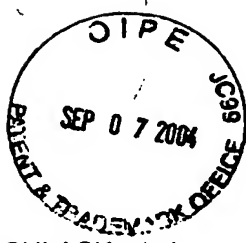


COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, VA 22313-1450



Docket No.: 200.1134CON  
Date: September 2, 2004

In re application of: Benjamin OSHLACK, et al.  
Serial No.: 10/747,865  
Filed: December 29, 2003  
For: **CONTROLLED-RELEASE COMPOSITIONS CONTAINING OPIOID AGONIST AND ANTAGONIST**

Sir:

Transmitted herewith is an **Information Disclosure Statement** in the above-identified application.

- ☐ Small entity status of this application under 37 C.F.R. 1.9 and 1.27 has been established by a verified statement previously submitted.
- ☐ A verified statement to establish small entity status under 37 C.F.R. 1.9 and 1.27 is enclosed.
- ☐ No fee for additional claims is required.
- ☐ A filing fee for additional claims calculated as shown below, is required:

| (Col. 1)   |              | (Col. 2)   |         | SMALL ENTITY |     | OR | LARGE ENTITY |     |
|--|--------------|------------|---------|--------------|-----|----|--------------|-----|
| FOR:   | REMAINING    | HIGHEST    |         | RATE         | FEE |    | RATE         | FEE |
|  | AFTER        | PREVIOUSLY | PRESENT |              |     |    |              |     |
|  | AMENDMENT    | PAID FOR   | EXTRA   |              |     |    |              |     |
| TOTAL CLAIMS   | * Minus 20** | =          |         | x \$ 9       | \$  |    | x \$ 18      | \$  |
| INDEP. CLAIMS  | * Minus 3*** | =          | 0       | x \$ 42      | \$  |    | x \$ 84      | \$  |
| <input type="checkbox"/> FIRST PRESENTATION OF MULTIPLE DEP. CLAIM |              |            |         | + \$140      | \$  |    | + \$280      | \$  |

TOTAL: \$ OR TOTAL: \$

- \* If the entry in Co. 1 is less than the entry in Col. 2, write "0" in Col. 3.
- \*\* If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, write "20" in this space.
- \*\*\* If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, write "3" in this space.

- ☒ Also transmitted herewith are:
- ☐ Petition for extension under 37 C.F.R. 1.136 (in duplicate)
- ☒ Other: PTO form 1449 (24 pages),  
references cited and Exhibit A
- ☐ Check(s) in the amount of \$ . 00 is/are attached to cover:
- ☐ Filing fee for additional claims under 37 C.F.R. 1.16
- ☐ Petition fee for extension under 37 C.F.R. 1.136
- ☐ Other:
- ☒ The Assistant Commissioner is hereby authorized to charge payment of the following fees associated with this communication or credit any overpayment to Deposit Account No. 50-0552.
- ☒ Any filing fee under 37 C.F.R. 1.16 for the presentation of additional claims which are not paid by check submitted herewith.
- ☒ Any patent application processing fees under 37 C.F.R. 1.17.
- ☒ Any petition fees for extension under 37 C.F.R. 1.136 which are not paid by check submitted herewith, and it is hereby requested that this be a petition for an automatic extension of time under 37 CFR 1.136.

Robert J. Paradiso, Reg. No. 41,240  
DAVIDSON, DAVIDSON & KAPPEL, LLC  
485 Seventh Avenue, 14<sup>th</sup> Floor  
New York, New York 10018  
Tel: (212) 736-1940  
Fax: (212) 736-2427

I hereby certify that this correspondence and/or documents referred to as attached therein and/or fee are being deposited with the United States Postal Service as "first class mail" in an envelope addressed to "Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450" on September 2, 2004.

DAVIDSON, DAVIDSON & KAPPEL, LLC

BY

Elizabeth Pietrowski

BEST AVAILABLE COPY



200.1134CON

**UNITED STATES PATENT AND TRADEMARK OFFICE**

Examiner: To be determined; Art Unit: 1614

Re: Application of: Benjamin OSHLACK et al.  
Serial No.: 10/747,865  
Filed: December 29, 2003  
For: **CONTROLLED-RELEASE COMPOSITIONS  
CONTAINING OPIOID AGONIST AND  
ANTAGONIST**

**INFORMATION DISCLOSURE  
STATEMENT UNDER 37 C.F.R. § 1.56**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

September 2, 2004

Sir:

In accordance with the provisions of 37 C.F.R. § 1.97, Applicants hereby make of record the documents listed on the accompanying Form PTO-1449 (24 sheets) for consideration by the Examiner in connection with the examination of the above-identified patent application.

Pursuant to 37 C.F.R. § 1.98 (a), the foreign patent documents listed on sheet 21 of the attached Form PTO-1449, which were not cited in the parent application, references UJ and UK, are enclosed. In accordance with the provisions of 37 C.F.R. § 1.98 (d), the references listed on pages 1-24 which were previously submitted in the parent application, U.S. Serial No. 09/781,076, are not enclosed. If it is determined that any of the listed references were not submitted in the parent application or presently enclosed, the Examiner is requested to contact the undersigned so that a copy can be forwarded.

Applicants also respectfully advise the Examiner of the following U.S. Patents and co-pending U.S. Patent Applications which are commonly assigned to the owners of the instant application:

U.S. Application Serial No. 10/694,559, entitled “Opioid Agonist/Antagonist Combinations”, filed October 27, 2003, which is a continuation of U.S. Application Serial No. 10/244,783, entitled “Opioid Agonist/Antagonist Combinations”, filed September 16, 2002, now U.S. Patent No. 6,696,066, issued February 24, 2004, which is a continuation of U.S. Application Serial No. 09/815,167, entitled “Opioid Agonist/Antagonist Combinations”, filed March 22, 2001, now U.S. Patent No. 6,475,494, issued November 5, 2002, which is a continuation of U.S. Application Serial No. 09/218,662, entitled “Opioid Agonist/Antagonist Combinations”, filed December 22, 1998, now U.S. Patent No. 6,277,384, issued August 21, 2001;

U.S. Application Serial No. 10/389,238, entitled “Naltrexone Hydrochloride Compositions”, filed March 14, 2003;

U.S. Application Serial No. 10/700,906, entitled “Tamper Resistant Oral Opioid Agonist Formulations”, filed October 30, 2003 and U.S. Application Serial Nos. 10/700,893, 10/700,861, 10/701,041 and 10/689,866, entitled “Tamper Resistant Oral Opioid Agonist Formulations”, filed November 4, 2003, which are continuations of U.S. Application Serial No. 09/781,081, entitled “Tamper Resistant Oral Opioid Agonist Formulations”, filed February 8, 2001, now U.S. Patent No. 6,696,088, issued February 24, 2004;

U.S. Application Serial No. 09/992,936, entitled “Opioid Agonist/Opioid Antagonist Acetaminophen Combination”, filed November 5, 2001, which is a continuation of U.S. Application Serial No. 09/503,020 filed February 11, 2000 entitled “Opioid Agonist/Opioid Antagonist/Acetaminophen Combinations”, now U.S. Patent No. 6,375,957, issued April 23, 2002, which is a continuation in part of U.S. Application Serial No. 09/218,662, “Opioid Agonist/Antagonist Combinations”, filed December 22, 1998, now U.S. Patent No. 6,277,384, issued August 21, 2001, listed as reference WG on the attached Form PTO-1449;

U.S. Application Serial No. 10/665,735, entitled “A Method of Preventing Abuse of Opioid Dosage Forms”, filed September 18, 2003, which is a continuation of U.S. Application Serial No. 09/815,162, now U.S. Patent No. 6,627,635, issued September 30, 2003, listed as reference XI on the attached Form PTO-1449;

U.S. Application Serial No. 10/827,623, entitled “Pharmaceutical Products”, filed April 19, 2004;

U.S. Application Serial No. 10/213,919, entitled “Opioid Agonist Formulations with Releasable and Sequestered Antagonist”, filed August 6, 2002;

U.S. Application Serial No. 10/214,408, entitled “Sequestered Antagonist Formulations”, filed August 6, 2002; and

U.S. Application Serial No. 10/199,972, entitled “Pharmaceutical Combinations of Oxycodone and Naloxone”, filed July 18, 2002.

Pursuant to 37 C.F.R. § 1.98 (a)(2)(iii), the Examiner’s attention is directed to Exhibit A, attached herewith, which contains the following:

(i) the claims of pending U.S. Application Serial No. 09/992,936, which has the same specification as U.S. Patent No. 6,375,957, listed as reference XE on the attached Form PTO-1449;

(ii) the claims of pending U.S. Application Serial No. 10/665,735, which has the same specification as U.S. Patent No. 6,627,635, listed as reference XI on the attached Form PTO-1449;

(iii) the claims of pending U.S. Application Serial Nos. 10/700,906, 10/700,893, 10/700,861, 10/701,041 and 10/689,866, which have the same specification as U.S. Patent No. 6,696,088, listed as reference XK on the attached Form PTO-1449;

(iv) the claims of pending U.S. Application Serial No. 10/694,559, which has the same specification as U.S. Patent No. 6,696,066, listed as reference XL on the attached Form PTO-1449;

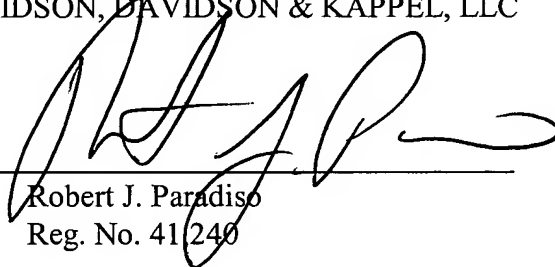
(v) the specifications and claims for pending U.S. Applications Serial Nos. 10/213,919, 10/214,408, 10/199,972, 10/827,623 and 10/389,238.

It is respectfully requested that the references cited in the accompanying Form PTO-1449 (24 sheets) be considered and made of record.

This Information Disclosure Statement is filed under 37 C.F.R. § 1.97 (b), before the mailing of a first Office Action on the merits. Accordingly, no fee is believed due. In the event any additional fee is due or any overpayment made in connection with the filing of this Information Disclosure Statement, the Commissioner is hereby authorized to charge said deficiency or credit overpayment to our Deposit Account No. 50-0552.

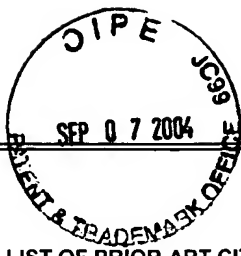
Respectfully submitted,  
DAVIDSON, DAVIDSON & KAPPEL, LLC

By



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Reg. No. 41240

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|   |    |   |   |  |   |                          |   |   |            |                   |       |          |                               |    |
|---|----|---|---|--|---|--------------------------|---|---|------------|-------------------|-------|----------|-------------------------------|----|
| FORM PTO-1449<br>(REV. 7-80)  |    | U.S. DEPARTMENT OF COMMERCE<br>PATENT AND TRADEMARK OFFICE  |   | ATTY. DOCKET NO.:<br>200.1134CON         |   | SERIAL NO.:<br>10747,865 |   |   |            |                   |       |          |                               |    |
| LIST OF PRIOR ART CITED BY APPLICANT<br><br>(Use several sheets if necessary)   |    |   |   | APPLICANT(S):<br>Benjamin OSHLACK et al. |   |                          |   |   |            |                   |       |          |                               |    |
|   |    |   |   | FILING DATE:<br>December 29, 2003        |   | GROUP:<br>1614           |   |   |            |                   |       |          |                               |    |
| U.S. PATENT DOCUMENTS   |    |   |   |  |   |                          |   |   |            |                   |       |          |                               |    |
| *EXAMINER<br>INITIAL  |    | DOCUMENT NUMBER   |   |  |   |                          |   |   | DATE       | NAME              | CLASS | SUBCLASS | FILING DATE<br>IF APPROPRIATE |    |
|   | AA | 2   | 7 | 7  | 0 | 5                        | 6 | 9 | 11/56      | Fromherz et al.   | 167   | 65       |                               |    |
|   | AB | 3   | 1 | 3  | 3 | 1                        | 3 | 2 | 05/12/64   | Loeb, et al.      | 264   | 49       |                               |    |
|   | AC | 3   | 1 | 7  | 3 | 8                        | 7 | 6 | 03/16/65   | Zobrist           | 252   | 137      |                               |    |
|   | AD | 3   | 2 | 7  | 6 | 5                        | 8 | 6 | 10/04/66   | Rosaen            | 210   | 90       |                               |    |
|   | AE | 3   | 3 | 3  | 2 | 9                        | 5 | 0 | 7/67       | Blumberg et al.   | 260   | 285      |                               |    |
|   | AF | 3   | 4 | 9  | 3 | 6                        | 5 | 7 | 2/70       | Lewenstein et al. | 424   | 260      |                               |    |
|   | AG | 3   | 6 | 7  | 6 | 5                        | 5 | 7 | 7/72       | Lachman et al.    | 424   | 260      |                               |    |
|   | AH | 3   | 7 | 7  | 3 | 9                        | 5 | 5 | 11/73      | Pachter et al.    | 424   | 260      |                               |    |
|   | AI | 3   | 8 | 7  | 9 | 5                        | 5 | 5 | 4/75       | Pachter et al.    | 424   | 260      |                               |    |
| FOREIGN PATENT DOCUMENTS  |    |   |   |  |   |                          |   |   |            |                   |       |          |                               |    |
|   |    | DOCUMENT NUMBER   |   |  |   |                          |   |   | DATE       | COUNTRY           | CLASS | SUBCLASS | TRANSLATION                   |    |
|   |    |   |   |  |   |                          |   |   |            |                   |       |          | YES                           | NO |
|   | AJ | 8   | 3 | 0  | 3 | 1                        | 9 | 7 | 9/83       | WO                | A61K  | 9/22     |                               |    |
|   | AK | 9   | 0 | 0  | 4 | 9                        | 6 | 5 | 05/17/1990 | WO                | A61K  | 31/485   |                               |    |
|   | AL | 9   | 4 | 0  | 6 | 4                        | 2 | 6 | 3/94       | WO                | A61K  | 31/46    |                               |    |
|   | AM | 9   | 5 | 0  | 3 | 8                        | 0 | 4 | 2/95       | WO                | A61K  | 31/485   |                               |    |
|   | AN | 9   | 6 | 0  | 2 | 2                        | 5 | 1 | 2/96       | WO                | A61K  | 31/485   |                               |    |
| OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)  |    |   |   |  |   |                          |   |   |            |                   |       |          |                               |    |
|   | AO | Foss, J.F., et al. Abstract, "Prevention of Apomorphine- or Cisplatin- induced emesis in the dog by combination of Methylalntrexone and Morphine", Cancer Chemother Pharmacol (1998); 42(4):287-91. |   |  |   |                          |   |   |            |                   |       |          |                               |    |
|   | AP | Yuan et al., "Efficacy of Orally Administered Methylalntrexone in Decreasing Subjective Effects After Intravenous Morphine", Drug and Alcohol Dependence (1998); 52:161-165.                        |   |  |   |                          |   |   |            |                   |       |          |                               |    |
|   | AQ | Gan et al., "Opioid-Sparing Effects of a Low-Dose Infusion of Naloxone in Patient-Administered Morphine Sulfate," Anesthesiology (1997), 87(5):1075-1080.   |   |  |   |                          |   |   |            |                   |       |          |                               |    |
|   | AR | Shen et al., "Ultra-Low Doses of Naltrexone or Etorphine Increase Morphine's Antinociceptive Potency and Attenuate Tolerance/Dependence in Mice," Brain Research (1997), 757:176-190.               |   |  |   |                          |   |   |            |                   |       |          |                               |    |
|   | AS | Yuan et al., "The Safety and Efficacy of Oral Methylalntrexone in Preventing Morphine-induced Delay in Oral-Cecal Transit Time", Clinical Trials and Therapeutics (1997), 61:467-475.               |   |  |   |                          |   |   |            |                   |       |          |                               |    |
|   | AT | Mendelson J., et al, "Buprenorphine and Naloxone Interactions in Opiate Dependent Volunteers," Clin. Phar. Ther. (1996), 60:105-114.  |   |  |   |                          |   |   |            |                   |       |          |                               |    |
|   | AU | Walsh et al., "Effects of Naltrexone on Response to Intravenous Cocain, Hydromorphone and their Combination in Humans," (1996).   |   |  |   |                          |   |   |            |                   |       |          |                               |    |
| EXAMINER  |    |   |   |  |   |                          |   |   |            | DATE CONSIDERED   |       |          |                               |    |
| *EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. |    |   |   |  |   |                          |   |   |            |                   |       |          |                               |    |

| FORM PTO-1449<br>(REV. 7-80)  |    | U.S. DEPARTMENT OF COMMERCE<br>PATENT AND TRADEMARK OFFICE   |   |   |   | ATTY. DOCKET NO.:<br>200.1134CON         |   | SERIAL NO.:<br>10/747,865 |            |                 |       |          |                               |    |
|---|----|--|---|---|---|--|---|---------------------------|------------|-----------------|-------|----------|-------------------------------|----|
| <b>LIST OF PRIOR ART CITED BY APPLICANT</b>   |    |  |   |   |   | APPLICANT(S):<br>Benjamin OSHLACK et al. |   |                           |            |                 |       |          |                               |    |
| (Use several sheets if necessary)   |    |  |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   |    |  |   |   |   | FILING DATE:<br>December 29, 2003        |   | GROUP:<br>1614            |            |                 |       |          |                               |    |
| <b>U.S. PATENT DOCUMENTS</b>  |    |  |   |   |   |  |   |                           |            |                 |       |          |                               |    |
| *EXAMINER<br>INITIAL  |    | DOCUMENT NUMBER  |   |   |   |  |   |                           | DATE       | NAME            | CLASS | SUBCLASS | FILING DATE<br>IF APPROPRIATE |    |
|   | BA | 3  | 9 | 1 | 6 | 8  | 8 | 9                         | 11/04/1975 | Russell         | 128   | 145.8    |                               |    |
|   | BB | 3  | 9 | 6 | 5 | 2  | 5 | 6                         | 06/22/1976 | Leslie          | 424   | 22       |                               |    |
|   | BC | 3  | 9 | 6 | 6 | 9  | 4 | 0                         | 6/76       | Pachter et al.  | 424   | 260      |                               |    |
|   | BD | 4  | 1 | 7 | 6 | 1  | 8 | 6                         | 11/79      | Goldberg        | 424   | 260      |                               |    |
|   | BE | 4  | 2 | 3 | 7 | 1  | 4 | 0                         | 12/02/1980 | Dudzinski       | 424   | 260      |                               |    |
| <b>FOREIGN PATENT DOCUMENTS</b>   |    |  |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   |    | DOCUMENT NUMBER  |   |   |   |  |   |                           | DATE       | COUNTRY         | CLASS | SUBCLASS | TRANSLATION                   |    |
|   |    |  |   |   |   |  |   |                           |            |                 |       |          | YES                           | NO |
|   | BF | 9  | 7 | 3 | 3 | 5  | 6 | 6                         | 9/97       | WO              | A61K  | 9/20     |                               |    |
|   | BG | 9  | 8 | 3 | 5 | 6  | 7 | 9                         | 8/98       | WO              | A61K  | 31/485   |                               |    |
|   | BH | 9  | 9 | 3 | 2 | 1  | 2 | 0                         | 7/99       | WO              | A61K  | 31/485   |                               |    |
|   | BI | 0  | 0 | 0 | 1 | 3  | 7 | 7                         | 01/13/2000 | WO              | A61K  | 31/00    |                               |    |
|   | BJ | 8  | 7 | 0 | 1 | 2  | 8 | 2                         | 03/12/1987 | WO              | A61K  | 31/485   |                               |    |
| <b>OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)</b>   |    |  |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   | BK | Chih-Cheng Chien, et al., "Sigma Antagonists Potentiate Opioid Analgesia in Rats", Neuroscience Letters 190 (1995), 137-139.   |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   | BL | Crain et al., "Ultra-Low Concentrations of Naloxone Selectively Antagonize Excitatory Effects of Morphine on Sensory Neurons, Thereby Increasing Its Antinociceptive Potency and Attenuating Tolerance/Dependence During Chronic Cotreatment," Proc. Natl. Acad. Sci. USA (1995) 92:10540-10544. |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   | BN | Hanson, Analgesic, Antipyretic and Anti-Inflammatory Drugs in Remington's Science and Practice of Pharmacy (1995), 2:1207.   |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   | BO | Talwin NX, Physician's Desk Reference 48 <sup>th</sup> Ed. (1994) Montvale, NJ 2120-2121.  |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   | BP | Foss et al., "Dose related Antagonism of the Emetic Effect of Morphine by Methylnaltrexone in Dogs", J. Clin Pharmacol (1993), 33:747-751  |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   | BQ | Holmes et al., "Inhibiting Spinal Dynorphin A Component Enhances Intrathecal Morphine Antinociception in Mice", Anesth. Analg. (1993), 77:1166-73.   |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   | BR | Miakowski et al., "Inhibition of Spinal Opioid Analgesia by Supraspinal Administration of Selective Opioid Antagonists", Brain Research (1992), 30:263-274.  |   |   |   |  |   |                           |            |                 |       |          |                               |    |
| EXAMINER  |    |  |   |   |   |  |   |                           |            | DATE CONSIDERED |       |          |                               |    |
| *EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. |    |  |   |   |   |  |   |                           |            |                 |       |          |                               |    |

| FORM PTO-1449<br>(REV. 7-80)  |    | U.S. DEPARTMENT OF COMMERCE<br>PATENT AND TRADEMARK OFFICE   |   |   |   | ATTY. DOCKET NO.:<br>200.1134CON         |   | SERIAL NO.:<br>10/747,865 |            |                   |       |          |                               |    |
|---|----|--|---|---|---|--|---|---------------------------|------------|-------------------|-------|----------|-------------------------------|----|
| <b>LIST OF PRIOR ART CITED BY APPLICANT</b>   |    |  |   |   |   | APPLICANT(S):<br>Benjamin OSHLACK et al. |   |                           |            |                   |       |          |                               |    |
| (Use several sheets if necessary)   |    |  |   |   |   |  |   |                           |            |                   |       |          |                               |    |
|   |    |  |   |   |   | FILING DATE:<br>December 29, 2003        |   | GROUP:<br>1614            |            |                   |       |          |                               |    |
| <b>U.S. PATENT DOCUMENTS</b>  |    |  |   |   |   |  |   |                           |            |                   |       |          |                               |    |
| *EXAMINER<br>INITIAL  |    | DOCUMENT NUMBER  |   |   |   |  |   |                           | DATE       | NAME              | CLASS | SUBCLASS | FILING DATE<br>IF APPROPRIATE |    |
|   | CA | 4  | 2 | 8 | 5 | 9  | 8 | 7                         | 08/25/1981 | Ayer, et al.      | 427   | 3        |                               |    |
|   | CB | 4  | 3 | 6 | 6 | 3  | 1 | 0                         | 12/28/1982 | Leslie            | 536   | 56       |                               |    |
|   | CC | 4  | 4 | 0 | 1 | 6  | 7 | 2                         | 8/83       | Portoghese et al. | 424   | 260      |                               |    |
|   | CD | 4  | 4 | 4 | 3 | 4  | 2 | 8                         | 04/17/1984 | Oshlack et al.    | 424   | 22       |                               |    |
|   | CE | 4  | 4 | 5 | 1 | 4  | 7 | 0                         | 5/84       | Ganti             | 424   | 260      |                               |    |
|   | CF | 4  | 4 | 5 | 7 | 9  | 3 | 3                         | 7/84       | Gordon et al.     | 424   | 260      |                               |    |
|   | CG | 4  | 4 | 6 | 4 | 3  | 7 | 8                         | 8/84       | Hussain et al.    | 424   | 260      |                               |    |
| <b>FOREIGN PATENT DOCUMENTS</b>   |    |  |   |   |   |  |   |                           |            |                   |       |          |                               |    |
|   |    | DOCUMENT NUMBER  |   |   |   |  |   |                           | DATE       | COUNTRY           | CLASS | SUBCLASS | TRANSLATION                   |    |
|   |    |  |   |   |   |  |   |                           |            |                   |       |          | YES                           | NO |
|   | CH | 0  | 1 | 3 | 2 | 1  | 8 | 0                         | 05/10/2001 | WO (A2)           | A61K  | 31/485   |                               |    |
|   | CI | 0  | 1 | 6 | 8 | 0  | 8 | 0                         | 09/20/2001 | WO (A2)           | A61K  | 31/00    |                               |    |
|   | CJ | 0  | 1 | 3 | 7 | 7  | 8 | 5                         | 05/31/2001 | WO (A2)           | A61K  |          |                               |    |
|   | CK | 0  | 1 | 5 | 2 | 8  | 5 | 1                         | 07/26/2001 | WO (A1)           | A61K  | 31/485   |                               |    |
|   | CL | 0  | 1 | 8 | 5 | 2  | 5 | 7                         | 11/15/2001 | WO (A2)           | A61P  |          |                               |    |
| <b>OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)</b>   |    |  |   |   |   |  |   |                           |            |                   |       |          |                               |    |
|   | CM | Weinhold et al., "Buprenorphine Alone and in Combination with Naltrexone in Non-Dependent Humans," Drug and Alcohol Dependence (1992), 30:263-274.                                       |   |   |   |  |   |                           |            |                   |       |          |                               |    |
|   | CN | Cappel et al., "Enhancement of Naloxone Induced Analgesia by Pretreatment with Morphine" Pharma. Bioch. & Behav. (1989), 34:425-427.   |   |   |   |  |   |                           |            |                   |       |          |                               |    |
|   | CO | Vaccarino et al., "Analgesia Produced by Normal Doses of Opioid Antagonists Alone and in Combination with Morphine", Pain (1989), 36:103-109.  |   |   |   |  |   |                           |            |                   |       |          |                               |    |
|   | CP | Gonzalez et al., "Naltrexone: A Review of its Pharmacodynamic and Pharmacokinetic Properties and Therapeutic Efficacy in the Management of Opioid Dependence," Drugs (1988), 35:192-213. |   |   |   |  |   |                           |            |                   |       |          |                               |    |
|   | CQ | Sunshine, et al., "Analgesic Efficacy of Pentazocine Versus a Pentazocine-Naloxone Combination Following Oral Administration," Clin. J. Pain (1988), 4:35-40.                            |   |   |   |  |   |                           |            |                   |       |          |                               |    |
|   | CR | Wang et al., "Crossover and Parallel Study of Oral Analgesics," J. Clin. Pharmacol (1981), 21:162-168.   |   |   |   |  |   |                           |            |                   |       |          |                               |    |
|   | CS | Translation of German patent application DE 43 25 465  |   |   |   |  |   |                           |            |                   |       |          |                               |    |
| EXAMINER  |    |  |   |   |   |  |   |                           |            | DATE CONSIDERED   |       |          |                               |    |
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| FORM PTO-1449<br>(REV. 7-80)  |    | U.S. DEPARTMENT OF COMMERCE<br>PATENT AND TRADEMARK OFFICE   |   | ATTY. DOCKET NO.:<br>200.1134CON         |   | SERIAL NO.:<br>10/747,865 |   |   |            |                     |       |          |                               |    |
| <b>LIST OF PRIOR ART CITED BY APPLICANT</b><br><br>(Use several sheets if necessary)  |    |  |   | APPLICANT(S):<br>Benjamin OSHLACK et al. |   |                           |   |   |            |                     |       |          |                               |    |
|   |    |  |   | FILING DATE:<br>December 29, 2003        |   | GROUP:<br>1614            |   |   |            |                     |       |          |                               |    |
| <b>U.S. PATENT DOCUMENTS</b>  |    |  |   |  |   |                           |   |   |            |                     |       |          |                               |    |
| *EXAMINER<br>INITIAL  |    | DOCUMENT NUMBER  |   |  |   |                           |   |   | DATE       | NAME                | CLASS | SUBCLASS | FILING DATE<br>IF APPROPRIATE |    |
|   | DA | 4  | 5 | 7  | 3 | 9                         | 9 | 5 | 3/86       | Chen et al.         | 604   | 896      |                               |    |
|   | DB | 4  | 5 | 8  | 2 | 8                         | 3 | 5 | 4/86       | Lewis et al.        | 514   | 282      |                               |    |
|   | DC | 4  | 6 | 0  | 8 | 3                         | 7 | 6 | 8/86       | Pasternak           | 514   | 282      |                               |    |
|   | DD | 4  | 6 | 6  | 1 | 4                         | 3 | 2 | 4/87       | Lewis et al.        | 514   | 282      |                               |    |
|   | DE | 4  | 7 | 1  | 9 | 2                         | 1 | 5 | 1/88       | Goldberg            | 514   | 282      |                               |    |
|   | DF | 4  | 7 | 3  | 0 | 0                         | 4 | 8 | 3/88       | Portoghese et al.   | 546   | 45       |                               |    |
|   | DG | 4  | 7 | 6  | 0 | 0                         | 6 | 9 | 7/88       | Rzeszotarski et al. | 514   | 282      |                               |    |
| <b>FOREIGN PATENT DOCUMENTS</b>   |    |  |   |  |   |                           |   |   |            |                     |       |          |                               |    |
|   |    | DOCUMENT NUMBER  |   |  |   |                           |   |   | DATE       | COUNTRY             | CLASS | SUBCLASS | TRANSLATION                   |    |
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|   | DH | 0  | 1 | 9  | 3 | 8                         | 5 | 2 | 12/31/2001 | WO (A2)             | A61K  | 31/00    |                               |    |
|   | DI | 0  | 9 | 1  | 3 | 1                         | 5 | 2 | 6/99       | EP                  | A61K  | 31/485   |                               |    |
|   | DJ | 0  | 6 | 4  | 7 | 4                         | 4 | 8 | 4/95       | EP                  | A61K  | 31/485   |                               |    |
|   | DK | 0  | 3 | 5  | 2 | 3                         | 6 | 1 | 1/90       | EP                  | A61K  | 31/485   |                               |    |
|   | DL | 0  | 2 | 0  | 5 | 2                         | 8 | 2 | 12/86      | EP                  | A61K  | 9/22     |                               |    |
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|   | DM | Alvarez-Fuentes, et al. "Effectiveness of Repeated Administration of a New Ora Naltrexone Controlled-Release System in Morphine Analgesia"; J. Pharm Pharmacol (2001), 53:1201-1205. |   |  |   |                           |   |   |            |                     |       |          |                               |    |
|   | DN | Alvarez-Fuentes, et al., "Preclinical Study of an Oral Controlled Release Naltrexone Complex in Mice"; J. Pharm Pharmacol (2000), 52:659-663.  |   |  |   |                           |   |   |            |                     |       |          |                               |    |
|   | DO | Archer, Sydney; "Historical Perspective on the Chemistry and Development of Naltrexone"; Naltrexone Research Monograph 28 (1980) p. 3-9.   |   |  |   |                           |   |   |            |                     |       |          |                               |    |
|   | DP | Baum et al., "The Impact of the Addition of Naloxone on the Use and Abuse of Pentazocine"; Public Health Reports (1987) Vol. 102, No. 4 p. 426-429.                                  |   |  |   |                           |   |   |            |                     |       |          |                               |    |
|   | DQ | Rapaka et al., "Discovery of Novel Opioid Medications"; NIDA Research Monograph 147 (1995) p. 55-83.   |   |  |   |                           |   |   |            |                     |       |          |                               |    |
|   | DR | Bloom et al., "Clinical Studies with Naloxone/Methadone in a Ratio of 1:20"; 5 <sup>th</sup> National Conference on Methadone Treatment (1973) Vol 2, p. 1342-1349.                  |   |  |   |                           |   |   |            |                     |       |          |                               |    |
| EXAMINER  |    |  |   |  |   |                           |   |   |            | DATE CONSIDERED     |       |          |                               |    |
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|   |    |   |   |   |   | FILING DATE:<br>December 29, 2003        |   | GROUP:<br>1614           |            |                 |       |          |                               |    |
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| *EXAMINER<br>INITIAL  | EA | DOCUMENT NUMBER   |   |   |   |  |   |                          | DATE       | NAME            | CLASS | SUBCLASS | FILING DATE<br>IF APPROPRIATE |    |
|   |    | 4   | 7 | 6 | 9 | 3  | 7 | 2                        | 9/88       | Kreek et al.    | 514   | 282      |                               |    |
|   | EB | 4   | 7 | 8 | 5 | 0  | 0 | 0                        | 11/88      | Kreek et al.    | 514   | 282      |                               |    |
|   | EC | 4   | 8 | 0 | 3 | 2  | 0 | 8                        | 2/89       | Pasternak       | 514   | 282      |                               |    |
|   | ED | 4   | 8 | 0 | 6 | 3  | 4 | 1                        | 2/89       | Chien et al.    | 424   | 448      |                               |    |
|   | EE | 4   | 8 | 0 | 6 | 5  | 4 | 3                        | 2/89       | Choi            | 514   | 464      |                               |    |
|   | EF | 4   | 8 | 0 | 6 | 5  | 5 | 8                        | 2/89       | Wuest et al.    | 514   | 381      |                               |    |
|   | EG | 4   | 8 | 2 | 8 | 8  | 3 | 6                        | 05/09/1989 | Elger et al.    | 424   | 419      |                               |    |
| <b>FOREIGN PATENT DOCUMENTS</b>   |    |   |   |   |   |  |   |                          |            |                 |       |          |                               |    |
|   |    | DOCUMENT NUMBER   |   |   |   |  |   |                          | DATE       | COUNTRY         | CLASS | SUBCLASS | TRANSLATION                   |    |
|   |    |   |   |   |   |  |   |                          |            |                 |       |          | YES                           | NO |
|   | EH | 0   | 1 | 9 | 3 | 3  | 5 | 5                        | 09/03/1986 | EP (A3)         | A61K  | 31/615   |                               |    |
|   | EI | 0   | 3 | 1 | 9 | 2  | 4 | 3                        | 06/07/1989 | EP (A1)         | A61K  | 31/485   |                               |    |
|   | EJ | 0   | 3 | 1 | 9 | 2  | 4 | 3                        | 11/07/1990 | EP (B1)         | A61K  | 31/485   |                               |    |
|   | EK | 19  | 6 | 5 | 1 | 5  | 5 | 1                        | 6/98       | DE              | A61K  | 31/485   |                               |    |
|   | EL | 29  | 7 | 1 | 9 | 7  | 0 | 4                        | 2/97       | DE              | A61K  | 31/485   | x                             |    |
| <b>OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)</b>   |    |   |   |   |   |  |   |                          |            |                 |       |          |                               |    |
|   | EM | Briscoe et al., "Methoclocinnamox: Time Course of Changes in Alfentanil-Reinforced Rhesus Monkeys"; Psychopharmacology (2000) 148:393-399.                          |   |   |   |  |   |                          |            |                 |       |          |                               |    |
|   | EN | Abstract of Bromm, et al., "A Sensitive Method to Evaluate Effects of Analgesics in Man"; Meth and Find Exptl Clin Pharmacol 5 (8) (1983) p. 545-551.               |   |   |   |  |   |                          |            |                 |       |          |                               |    |
|   | EO | Bullingham et al., "Clinical Pharmacokinetics of Narcotic Agonist-Antagonist Drugs"; Clinical Pharm (1983) 8: 332-343.  |   |   |   |  |   |                          |            |                 |       |          |                               |    |
|   | EP | Calimlim, et al. "Effect of Naloxone on the Analgesic Activity of Methadone in a 1:10 Oral Combination"; Clin Pharmacol and There (1974) Vol. 15; No. 6 pp.556-564. |   |   |   |  |   |                          |            |                 |       |          |                               |    |
|   | EQ | Caruso et al., "Methadone and Naloxone in Combination (Naldone®) for the Treatment if Heroin Addicts"; Bristol Laboratories, pp.1336-1341F.                         |   |   |   |  |   |                          |            |                 |       |          |                               |    |
|   | ER | Cherny, Nathan I., "Opioid Analgesics"; Drugs (1996) May:51 (5) pp. 713-737.  |   |   |   |  |   |                          |            |                 |       |          |                               |    |
|   | ES | Chiang, et al. "Clinical Evaluation of a Naltrexone Sustained-Release Preparation"; Drug and Alcohol Dependence (1985) 16, pp.1-8.                                  |   |   |   |  |   |                          |            |                 |       |          |                               |    |
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|   | FA | 4   | 8 | 3  | 4 | 9                         | 6 | 5 | 05/30/1989 | Martani et al.  | 424   | 488      |                               |    |
|   | FB | 4   | 8 | 3  | 4 | 9                         | 8 | 4 | 05/30/1989 | Goldie et al.   | 424   | 488      |                               |    |
|   | FC | 4   | 8 | 3  | 4 | 9                         | 8 | 5 | 05/30/1989 | Elger et al.    | 424   | 488      |                               |    |
|   | FD | 4   | 8 | 4  | 4 | 9                         | 0 | 7 | 07/04/1989 | Elger et al.    | 424   | 465      |                               |    |
|   | FE | 4   | 8 | 4  | 4 | 9                         | 0 | 9 | 07/04/1989 | Goldie et al.   | 424   | 480      |                               |    |
|   | FF | 4   | 8 | 4  | 4 | 9                         | 1 | 0 | 07/04/1989 | Leslie et al.   | 424   | 494      |                               |    |
|   | FG | 4   | 8 | 6  | 1 | 5                         | 9 | 8 | 8/89       | Oshlak et al.   | 424   | 468      |                               |    |
| <b>FOREIGN PATENT DOCUMENTS</b>   |    |   |   |  |   |                           |   |   |            |                 |       |          |                               |    |
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|   | FH | 4   | 3 | 2  | 5 | 4                         | 6 | 5 | 2/95       | DE              | A61K  | 31/485   |                               | x  |
|   | FI | 2   | 2 | 2  | 2 | 0                         | 3 | 9 | 11/72      | DE              | A61K  | 27/00    |                               |    |
|   | FJ | 9   | 8 | 2  | 5 | 6                         | 1 | 3 | 06/18/98   | WO              | A61K  | 31/485   | abstract                      |    |
|   | FK | 0   | 0 | 3  | 8 | 6                         | 4 | 9 | 07/06/00   | WO              | A61K  | 9/00     | abstract                      |    |
| <b>OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)</b>   |    |   |   |  |   |                           |   |   |            |                 |       |          |                               |    |
|   | FL | Chiang et al., "Kinetics of a Naltrexone Sustained-Release Preparation"; Clin Pharmacol Thera (1984) Vol 36 No. 5, pp.704-708.  |   |  |   |                           |   |   |            |                 |       |          |                               |    |
|   | FM | Comer et al., "Depot Naltrexone: Long-lasting Antagonism of the Effects Of Heroin un Humans"; Psychopharmacology (2002) 159, pp.351-360.  |   |  |   |                           |   |   |            |                 |       |          |                               |    |
|   | FN | Crabtree et al., "Review of Naltrexone, a long-acting Opiate Antagonist"; Clinical Pharmacy, Vol. 3 (1984) pp.273-280.  |   |  |   |                           |   |   |            |                 |       |          |                               |    |
|   | FO | Crain et al., "Antagonists of Excitatory Opioid Receptor Functions Enhance Morphine's Analgesic Potency and Attenuate Opioid Tolerance/dependence liability"; Dept. of Neuroscience, Albert Einstein College of Medicine Pain 82 (1999)pp.1-11.     |   |  |   |                           |   |   |            |                 |       |          |                               |    |
|   | FP | Crain et al., "Antagonists of Excitatory Opioid Receptor Functions Enhance Morphine's Analgesic Potency and Attenuate Opioid Tolerance/dependence liability"; Dept. of Neuroscience, Albert Einstein College of Medicine Pain 84 (2000) pp.121-131. |   |  |   |                           |   |   |            |                 |       |          |                               |    |
|   | FQ | Fink et al., "naloxone in Heroin Dependence"; Clin Pharm and Thera. Vol 9, No. 5;pp.568-577.  |   |  |   |                           |   |   |            |                 |       |          |                               |    |
|   | FR | Fishman et al., "Disposition of Naloxone-7,8- <sup>3</sup> H in Normal & Narcotic Dependent Men"; J. Pharm. And Exper. Thera (1973)Vol 10 No. 2;pp.575-580.   |   |  |   |                           |   |   |            |                 |       |          |                               |    |
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| *EXAMINER<br>INITIAL  |    | DOCUMENT NUMBER  |   |  |   |                           |   |   | DATE       | NAME                | CLASS | SUBCLASS | FILING DATE<br>IF APPROPRIATE |    |
|   | GA | 4  | 8 | 6  | 1 | 7                         | 8 | 1 | 8/89       | Goldberg            | 514   | 282      |                               |    |
|   | GB | 4  | 8 | 6  | 7 | 9                         | 8 | 5 | 09/19/1989 | Heafield et al.     | 424   | 461      |                               |    |
|   | GC | 4  | 8 | 7  | 3 | 0                         | 7 | 6 | 10/89      | Fishman et al.      | 412   | 10       |                               |    |
|   | GD | 4  | 8 | 8  | 2 | 3                         | 3 | 5 | 11/89      | Sinclair            | 514   | 282      |                               |    |
|   | GE | 4  | 8 | 8  | 9 | 6                         | 6 | 0 | 12/89      | Rzeszotarski et al. | 514   | 282      |                               |    |
|   | GF | 4  | 9 | 3  | 5 | 4                         | 2 | 8 | 6/90       | Lewis               | 514   | 282      |                               |    |
|   | GG | 4  | 9 | 4  | 0 | 5                         | 8 | 7 | 07/10/1990 | Jenkins et al.      | 424   | 480      |                               |    |
| <b>FOREIGN PATENT DOCUMENTS</b>   |    |  |   |  |   |                           |   |   |            |                     |       |          |                               |    |
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|   | GH | 00   | 1 | 5  | 8 | 4                         | 7 | 7 | 8/16/01    | WO                  | A61P  |          | abstract                      |    |
| <b>OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)</b>   |    |  |   |  |   |                           |   |   |            |                     |       |          |                               |    |
|   | GI | Fraser, Albert D., et al., "Clinical Toxicology of Drugs Used in the Treatment of Opiate Dependency"; Clinical Toxicology I (1990) Vol 10, No. 2; pp.375-386.  |   |  |   |                           |   |   |            |                     |       |          |                               |    |
|   | GJ | Freye et al., "Effects of Tramadol and Tilidine/Naloxone on Oral-Caecal Transit & Pupillary light Reflex"; Arzneimittel-Forsch/Drug Res. 50(I)(2000)pp. 24-30. |   |  |   |                           |   |   |            |                     |       |          |                               |    |
|   | GK | Fudala, et al., "Effects of Buprenorphine and Naloxone in Morphine-Stabilized Opioid Addicts"; Drug and Alcohol Dependence 50 (1998) pp. 1-8.                  |   |  |   |                           |   |   |            |                     |       |          |                               |    |
|   | GL | Fudala et al., "Human Pharmacology and Abuse Potential Of Nalmefene"; Clin Pharm and Thera (1991) Vol 49, 3, pp. 300-306.                                      |   |  |   |                           |   |   |            |                     |       |          |                               |    |
|   | GM | Gal et al., "Prolonged Blockade of Opioid Effect with Oral Nalmefene"; Clin Pharm and Thera (1986) pp. 537-542.  |   |  |   |                           |   |   |            |                     |       |          |                               |    |
|   | GN | Gerra et al., "Clonidine and Opiate Receptor Antagonists in the Treatment of Heroin Addiction"; J. Substance Abuse Treatment (1995) Vol 12, 1, pp. 35-41.      |   |  |   |                           |   |   |            |                     |       |          |                               |    |
|   | GO | Ghodse, et al., "Opioid analgesics and Narcotic Antagonists"; Side Effects of Drugs (2000) Annual 23, chpt 8 pp. 96-113.                                       |   |  |   |                           |   |   |            |                     |       |          |                               |    |
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|   |    |  |   | FILING DATE:<br>December 29, 2003        |   | GROUP:<br>1614            |   |   |            |                  |       |          |                               |    |
| <b>U.S. PATENT DOCUMENTS</b>  |    |  |   |  |   |                           |   |   |            |                  |       |          |                               |    |
| *EXAMINER<br>INITIAL  |    | DOCUMENT NUMBER  |   |  |   |                           |   |   | DATE       | NAME             | CLASS | SUBCLASS | FILING DATE<br>IF APPROPRIATE |    |
|   | HA | 4  | 2 | 0  | 0 | 0                         | 9 | 8 | 04/29/1980 | Ayer, et al.     | 128   | 260      |                               |    |
|   | HB | 4  | 9 | 7  | 0 | 0                         | 7 | 5 | 11/13/1990 | Oshlak           | 424   | 451      |                               |    |
|   | HC | 4  | 9 | 8  | 7 | 1                         | 3 | 6 | 01/22/1991 | Kreek et al.     | 514   | 282      |                               |    |
|   | HD | 4  | 9 | 9  | 6 | 3                         | 4 | 1 | 02/05/1991 | Goldie et al.    | 424   | 484      |                               |    |
|   | HE | 5  | 0 | 7  | 1 | 6                         | 4 | 6 | 12/10/1991 | Malkowska et al. | 424   | 497      |                               |    |
|   | HF | 5  | 0 | 7  | 5 | 3                         | 4 | 1 | 12/91      | Mendelson et al. | 514   | 282      |                               |    |
|   | HG | 5  | 0 | 8  | 6 | 0                         | 5 | 8 | 2/92       | Sinclair et al.  | 514   | 282      |                               |    |
| <b>FOREIGN PATENT DOCUMENTS</b>   |    |  |   |  |   |                           |   |   |            |                  |       |          |                               |    |
|   |    | DOCUMENT NUMBER  |   |  |   |                           |   |   | DATE       | COUNTRY          | CLASS | SUBCLASS | TRANSLATION                   |    |
|   |    |  |   |  |   |                           |   |   |            |                  |       |          | YES                           | NO |
|   | HH | 00   | 1 | 8  | 5 | 1                         | 5 | 0 | 11/15/01   | WO               | A61K  | 31/00    |                               |    |
| <b>OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)</b>   |    |  |   |  |   |                           |   |   |            |                  |       |          |                               |    |
|   | HI | Glatt, William, M.D. FACP, "A New Method for Detoxifying Opioid-Dependent Patients"; J. Substance Abuse Treatment (1999) Vol.17, No.3, pp. 193-197                   |   |  |   |                           |   |   |            |                  |       |          |                               |    |
|   | HJ | Gold, et al. "Rapid Opioid Detoxification During General Anesthesia"; Anesthesiology (1999) Vol 91, No 6, pp. 1639-1647.   |   |  |   |                           |   |   |            |                  |       |          |                               |    |
|   | HK | Greenwald, et al., "Comparative Clinical Pharmacology of Short-Acting $\mu$ Opioids in Drug Abusers"; J. Pharm and Exper Thera (1996) Vol 277, No 3, pp. 1228-1236.  |   |  |   |                           |   |   |            |                  |       |          |                               |    |
|   | HL | Gupta, et al., "Morphine Combined with Doxapram or Naloxone"; Anesthesia (1974) Vol 29, pp. 33-39.   |   |  |   |                           |   |   |            |                  |       |          |                               |    |
|   | HI | Richter et al., "Clinical Investigation on the Development of Dependence during Oral Therapy with Tramadol"; Arzneim-Forsch/Drug Res. 35 (No II)(1985)pp. 1742-1744. |   |  |   |                           |   |   |            |                  |       |          |                               |    |
|   | HN | Rosen et al., "The effect of Lamotrigine on Naloxone-precipitated Opiate withdrawal"; Drug and Alcohol Dependence (1998) Vol 52, pp. 173-176.                        |   |  |   |                           |   |   |            |                  |       |          |                               |    |
|   | HO | Rosen et al., "A Pilot Study of Dextromethorphan in Naloxone-Precipitated Opiate Withdrawal"; European J. of Pharm. (1996) Vol 307, pp. 251-257.                     |   |  |   |                           |   |   |            |                  |       |          |                               |    |
| EXAMINER  |    |  |   |  |   |                           |   |   |            | DATE CONSIDERED  |       |          |                               |    |
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|---|----|--|---|---|---|--|---|---------------------------|------------|-----------------|-------|----------|-------------------------------|----|
| FORM PTO-1449<br>(REV. 7-80)  |    | U.S. DEPARTMENT OF COMMERCE<br>PATENT AND TRADEMARK OFFICE   |   |   |   | ATTY. DOCKET NO.:<br>200.1134CON         |   | SERIAL NO.:<br>10/747,865 |            |                 |       |          |                               |    |
| <b>LIST OF PRIOR ART CITED BY APPLICANT</b><br><br>(Use several sheets if necessary)  |    |  |   |   |   | APPLICANT(S):<br>Benjamin OSHLACK et al. |   |                           |            |                 |       |          |                               |    |
|   |    |  |   |   |   | FILING DATE:<br>December 29, 2003        |   | GROUP:<br>1614            |            |                 |       |          |                               |    |
| <b>U.S. PATENT DOCUMENTS</b>  |    |  |   |   |   |  |   |                           |            |                 |       |          |                               |    |
| *EXAMINER<br>INITIAL  | IA | DOCUMENT NUMBER  |   |   |   |  |   |                           | DATE       | NAME            | CLASS | SUBCLASS | FILING DATE<br>IF APPROPRIATE |    |
|   | IA | 5  | 0 | 9 | 1 | 1  | 8 | 9                         | 02/25/1992 | Heafield et al. | 424   | 457      |                               |    |
|   | IB | 5  | 0 | 9 | 6 | 7  | 1 | 5                         | 3/92       | Sinclair        | 424   | 449      |                               |    |
|   | IG | 5  | 1 | 0 | 2 | 8  | 8 | 7                         | 4/92       | Goldberg        | 514   | 282      |                               |    |
|   | ID | 4  | 1 | 6 | 4 | 0  | 2 | 0                         | 07/03/1979 | Ayer, et al.    | 424   | 15       |                               |    |
|   | IE | 5  | 1 | 4 | 9 | 5  | 3 | 8                         | 9/92       | Granger et al.  | 424   | 449      |                               |    |
|   | IF | 5  | 2 | 1 | 5 | 7  | 5 | 0                         | 06/01/1993 | Krishnamurthy   | 424   | 488      |                               |    |
|   | IG | 5  | 2 | 2 | 5 | 4  | 4 | 0                         | 7/93       | London et al.   | 514   | 535      |                               |    |
| <b>FOREIGN PATENT DOCUMENTS</b>   |    |  |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   |    | DOCUMENT NUMBER  |   |   |   |  |   |                           | DATE       | COUNTRY         | CLASS | SUBCLASS | TRANSLATION                   |    |
|   |    |  |   |   |   |  |   |                           |            |                 |       |          | YES                           | NO |
|   | IH | 00   | 0 | 6 | 7 | 7  | 3 | 9                         | 11/16/00   | WO              | A61K  | 31/00    |                               |    |
| <b>OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)</b>   |    |  |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   | IL | Schuh et al., "Buprenorphine, Morphine and Naloxone Effects during Ascending Morphine Maintenance in Humans"; J. Pharm and Exper Thera (1996) Vol 278, 2, pp. 836-846.                     |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   | IK | Schuh et al., "Onset, Magnitude and Duration of Opioid Blockade Produced by Buprenorphine and Naltrexone in Humans"; Psychopharmacology (1999) Vol 145, pp. 162-174.                       |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   | IL | Stevens et al., "Nonspecific Excitatory Effects of Morphine: Reverse-Order Precipitated Withdrawal and Dose-Dose Interactions"; Psychopharmacology (1981) Vol 75, pp. 210-211.             |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   | IM | Stine et al., "Reduction of Opiate Withdrawal-like Symptoms by Cocaine Abuse during Methadone and Buprenorphine Maintenance"; Am. J. Drug and Alcohol Abuse (1994) Vol 20, 4, pp. 445-458. |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   | IN | Stine et al., "Use of Drug Combinations in Treatment of Opioid Withdrawal"; J. Clinical Psych. (1992) Vol 12, No 3, pp. 203-209.   |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   | IO | Stoller et al., "Effects of buprenorphine/naloxone in opioid-dependent humans" Psychopharmacology (2001) Vol 154, pp. 230-242.   |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   | IP | Strain et al., "Acute Effects of Buprenorphine, hydromorphone and naloxone in methadone-maintained volunteers"; J. Pharm and Exper Thera (1992) Vol 261, No 3, pp. 985-993.                |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   | IQ | Strain et al., "Effects of buprenorphine versus buprenorphine/naloxone tablets in non-dependent opioid abusers"; Psychopharmacology (2000) Vol 148, pp. 374-383.                           |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   | IR | Strain et al., "Precipitated Withdrawal by Pentazocine in Methadone-Maintained Volunteers"; J. Pharm and Exper Thera (1993) Vol 267, No 2, pp. 624-634.                                    |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   | IS | Tai, et al., "Naltrexone: An Antagonist Therapy for Heroin Addiction"; NIDA (1997) 5 pages   |   |   |   |  |   |                           |            |                 |       |          |                               |    |
| EXAMINER  |    |  |   |   |   |  |   |                           |            | DATE CONSIDERED |       |          |                               |    |
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| FORM PTO-1449<br>(REV. 7-80)  |    | U.S. DEPARTMENT OF COMMERCE<br>PATENT AND TRADEMARK OFFICE  |   | ATTY. DOCKET NO.:<br>200.1134CON         |   | SERIAL NO.:<br>10/747,865 |   |   |            |                 |       |          |                               |    |
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| (Use several sheets if necessary)   |    |   |   |  |   |                           |   |   |            |                 |       |          |                               |    |
|   |    |   |   | FILING DATE:<br>December 29, 2003        |   | GROUP:<br>1614            |   |   |            |                 |       |          |                               |    |
| U.S. PATENT DOCUMENTS   |    |   |   |  |   |                           |   |   |            |                 |       |          |                               |    |
| *EXAMINER<br>INITIAL  |    | DOCUMENT NUMBER   |   |  |   |                           |   |   | DATE       | NAME            | CLASS | SUBCLASS | FILING DATE<br>IF APPROPRIATE |    |
|   | JA | 5   | 2 | 2  | 6 | 3                         | 3 | 1 | 07/13/1993 | Thompson et al. | 73    | 865.9    |                               |    |
|   | JB | 5   | 2 | 3  | 6 | 7                         | 1 | 4 | 8/93       | Lee et al.      | 424   | 449      |                               |    |
|   | JC | 5   | 2 | 5  | 6 | 6                         | 6 | 9 | 10/93      | Askanazi et al. | 514   | 282      |                               |    |
|   | JD | 5   | 2 | 6  | 6 | 3                         | 3 | 1 | 11/30/1993 | Oshlak et al.   | 424   | 468      |                               |    |
|   | JE | 5   | 2 | 7  | 3 | 7                         | 6 | 0 | 12/93      | Oshlak et al.   | 424   | 486      |                               |    |
|   | JF | 5   | 2 | 8  | 6 | 4                         | 9 | 3 | 02/15/1994 | Oshlak et al.   | 424   | 468      |                               |    |
|   | JG | 5   | 3 | 1  | 6 | 7                         | 5 | 9 | 12/93      | Rose et al.     | 424   | 10       |                               |    |
| FOREIGN PATENT DOCUMENTS  |    |   |   |  |   |                           |   |   |            |                 |       |          |                               |    |
|   |    | DOCUMENT NUMBER   |   |  |   |                           |   |   | DATE       | COUNTRY         | CLASS | SUBCLASS | TRANSLATION                   |    |
|   |    |   |   |  |   |                           |   |   |            |                 |       |          | YES                           | NO |
|   | JH | 00  | 0 | 5  | 1 | 5                         | 9 | 2 | 9/05/00    | WO              | A61K  | 31/14    |                               |    |
| OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)  |    |   |   |  |   |                           |   |   |            |                 |       |          |                               |    |
|   | JI | Umbricht et al., "Naltrexone shortened opioid detoxification with buprenorphine"; Drug and Alcohol Dependence (1999) Vol 56 pp. 181-190   |   |  |   |                           |   |   |            |                 |       |          |                               |    |
|   | JK | Vaccarino et al., "Enogenous Opiates: 1999"; Peptides 21 (2000) pp. 1975-2034.  |   |  |   |                           |   |   |            |                 |       |          |                               |    |
|   | JL | Wang et al., "Inverse Agonists and neutral antagonists at $\mu$ opioid receptor (MOR): possible role of basal receptor signaling in narcotic dependence"; J. Neurochemistry (2001) Vol 77, pp. 1590-1600.   |   |  |   |                           |   |   |            |                 |       |          |                               |    |
|   | JM | Way et al., "Responsivity to Naloxone during Morphine Dependence"; Annals New York Academy of Sciences, pp. 252-261.  |   |  |   |                           |   |   |            |                 |       |          |                               |    |
|   | JN | Weinberg et al., "Sublingual absorption of selected opioid analgesics"; Clin Pharm Thera (1988) Vol 44, No 3, pp. 335-342.  |   |  |   |                           |   |   |            |                 |       |          |                               |    |
|   | JO | Wells, et al., "In vivo Pharmacological Characterization of SoRI 9409, a Nonpeptidic Opioid $\mu$ -Agonist/ $\delta$ -Antagonist that Produces Limited Antinociceptive Tolerance and Attenuates Morphine Physical Dependence"; J. Pharm and Exper Thera (2001) Vol 297, No 2, pp. 597-605 |   |  |   |                           |   |   |            |                 |       |          |                               |    |
|   | JP | Wodak, Alex, "Drug Treatment for Opioid Dependence"; Australian Prescriber (2001) Vol 24, No 1, pp. 4-6.  |   |  |   |                           |   |   |            |                 |       |          |                               |    |
|   | JQ | Wright et al., "Acute physical dependence in Humans; repeated naloxone-precipitated withdrawal after a single-dose of methadone"; Drug and Alcohol Dependence (1991) Vol 27, pp. 139-148.   |   |  |   |                           |   |   |            |                 |       |          |                               |    |
|   | JR | Zhu et al., "Naltrexone-precipitated morphine withdrawal in infant rat is attenuated by acute administration of NOS inhibitors but not NMDA receptor antagonists"; Psychopharmacology (2000) Vol 150, pp. 325-336.  |   |  |   |                           |   |   |            |                 |       |          |                               |    |
| EXAMINER  |    |   |   |  |   |                           |   |   |            | DATE CONSIDERED |       |          |                               |    |
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| FORM PTO-1449<br>(REV. 7-80)  |    | U.S. DEPARTMENT OF COMMERCE<br>PATENT AND TRADEMARK OFFICE   |   |   | ATTY. DOCKET NO.:<br>200.1134CON         |   | SERIAL NO.:<br>10/747,865 |   |            |                   |       |          |                               |    |
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|   |    |  |   |   | FILING DATE:<br>December 29, 2003        |   | GROUP:<br>1614            |   |            |                   |       |          |                               |    |
| <b>U.S. PATENT DOCUMENTS</b>  |    |  |   |   |  |   |                           |   |            |                   |       |          |                               |    |
| *EXAMINER<br>INITIAL  |    | DOCUMENT NUMBER  |   |   |  |   |                           |   | DATE       | NAME              | CLASS | SUBCLASS | FILING DATE<br>IF APPROPRIATE |    |
|   | KA | 5  | 3 | 1 | 7  | 0 | 2                         | 2 | 5/94       | Borsodi et al.    | 514   | 282      |                               |    |
|   | KB | 5  | 3 | 2 | 1  | 0 | 1                         | 2 | 6/94       | Mayer et al.      | 514   | 25       |                               |    |
|   | KC | 5  | 3 | 2 | 4  | 3 | 5                         | 1 | 06/28/1994 | Oshlak et al.     | 106   | 153      |                               |    |
|   | KD | 5  | 3 | 3 | 6  | 6 | 9                         | 1 | 08/09/1994 | Raffa et al.      | 514   | 629      |                               |    |
|   | KE | 5  | 3 | 5 | 2  | 6 | 8                         | 0 | 10/94      | Portoghese et al. | 514   | 279      |                               |    |
|   | KF | 5  | 3 | 5 | 2  | 6 | 8                         | 3 | 10/94      | Mayer et al.      | 514   | 289      |                               |    |
|   | KG | 5  | 3 | 5 | 6  | 4 | 6                         | 7 | 10/18/1994 | Oshlak et al.     | 106   | 153      |                               |    |
| <b>FOREIGN PATENT DOCUMENTS</b>   |    |  |   |   |  |   |                           |   |            |                   |       |          |                               |    |
|   |    | DOCUMENT NUMBER  |   |   |  |   |                           |   | DATE       | COUNTRY           | CLASS | SUBCLASS | TRANSLATION                   |    |
|   |    |  |   |   |  |   |                           |   |            |                   |       |          | YES                           | NO |
|   | KH | 0  | 1 | 5 | 8  | 4 | 5                         | 1 | 08/19/2001 | WO (A1)           | A61K  | 31/485   |                               |    |
| <b>OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)</b>   |    |  |   |   |  |   |                           |   |            |                   |       |          |                               |    |
|   | KI | Han et al., "Mucocoadhesive buccal disks for novel nalbuphine prodrug controlled delivery; effect of formulation variable on drug release and mucocoadhesive performance"; International J. Pharm (1999) Vol 177, pp. 201-209.               |   |   |  |   |                           |   |            |                   |       |          |                               |    |
|   | KJ | Handal et al., "Naloxone"; Annals of Emergency Medicine (1983) Vol 12:7, pp. 438-445.  |   |   |  |   |                           |   |            |                   |       |          |                               |    |
|   | KK | Harris et al., "Buprenorphine and Naloxone co-administration in opiate dependent patients stabilized on sublingual buprenorphine"; Drug and Alcohol Dependence (2000) Vol 61, pp. 85-94.   |   |   |  |   |                           |   |            |                   |       |          |                               |    |
|   | KL | Hawkes et al., "Effect of enteric-release formulation of naloxone on intestinal transit in volunteers taking codeine"; Aliment Pharm Ther (2001) Vol 15, pp. 625-630.  |   |   |  |   |                           |   |            |                   |       |          |                               |    |
|   | KM | Högger et al., "Comparison of tilidine/naloxone, tramadol and bromfenac in experimental pain: a double-blind randomized crossover study in healthy human volunteers"; International J. Clin Pharm and Thera (1999) Vol 37, No 8, pp. 377-385 |   |   |  |   |                           |   |            |                   |       |          |                               |    |
|   | KN | Budd, Keith, "Clinical Use of Opioid Antagonists"; Bailliere's Clinical Anesthesiology (1987) Vol 1, No 4, pp. 993-1011.   |   |   |  |   |                           |   |            |                   |       |          |                               |    |
|   | KO | Crain et al., "Ultra-low concentrations of naloxone selectively antagonize excitatory effects of morphine on sensory neurons, thereby increasing its antinociceptive potency and attenuating tolerance/dependence                            |   |   |  |   |                           |   |            |                   |       |          |                               |    |
|   | KP | Howes et al., "The Pharmacology of TR5109, a new Narcotic Agonist/Antagonist Analgesic"; NIDA Research (1979) pp. 99-105.  |   |   |  |   |                           |   |            |                   |       |          |                               |    |
|   | KQ | Leeling et al., "Disposition and metabolism of codorphone in the rat, dog, and man"; Drug Metabolism and Disposition (1982) Vol 10, No 6, pp 649-653.  |   |   |  |   |                           |   |            |                   |       |          |                               |    |
| EXAMINER  |    |  |   |   |  |   |                           |   |            | DATE CONSIDERED   |       |          |                               |    |
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| <b>LIST OF PRIOR ART CITED BY APPLICANT</b><br><br>(Use several sheets if necessary)  |    |  |   |   |   | APPLICANT(S):<br>Benjamin OSHLACK et al. |   |                           |            |                    |       |          |                               |    |
|   |    |  |   |   |   | FILING DATE:<br>December 29, 2003        |   | GROUP:<br>1614            |            |                    |       |          |                               |    |
| <b>U.S. PATENT DOCUMENTS</b>  |    |  |   |   |   |  |   |                           |            |                    |       |          |                               |    |
| *EXAMINER<br>INITIAL  |    | DOCUMENT NUMBER  |   |   |   |  |   |                           | DATE       | NAME               | CLASS | SUBCLASS | FILING DATE<br>IF APPROPRIATE |    |
|   | LA | 5  | 3 | 5 | 6 | 9  | 0 | 0                         | 10/94      | Bihari et al.      | 514   | 282      |                               |    |
|   | LB | 5  | 3 | 7 | 6 | 6  | 6 | 2                         | 12/94      | Ockert             | 514   | 282      |                               |    |
|   | LC | 3  | 5 | 4 | 1 | 0  | 0 | 5                         | 11/17/1970 | Strathmann, et al. | 210   | 19       |                               |    |
|   | LD | 5  | 4 | 1 | 1 | 7  | 4 | 5                         | 05/02/1995 | Oshlack et al.     | 424   | 456      |                               |    |
|   | LE | 5  | 4 | 2 | 6 | 1  | 1 | 2                         | 06/95      | Zagon et al.       | 514   | 282      |                               |    |
|   | LF | 3  | 5 | 4 | 1 | 0  | 0 | 6                         | 11/17/1970 | Bixler, et al.     | 210   | 23       |                               |    |
|   | LG | 5  | 4 | 5 | 7 | 2  | 0 | 8                         | 10/95      | Portoghese et al.  | 546   | 35       |                               |    |
| <b>FOREIGN PATENT DOCUMENTS</b>   |    |  |   |   |   |  |   |                           |            |                    |       |          |                               |    |
|   |    | DOCUMENT NUMBER  |   |   |   |  |   |                           | DATE       | COUNTRY            | CLASS | SUBCLASS | TRANSLATION                   |    |
|   |    |  |   |   |   |  |   |                           |            |                    |       |          | YES                           | NO |
|   | LH | 0  | 8 | 8 | 0 | 3  | 5 | 2                         | 02/03/1998 | EP (B1)            | A61K  | 31/485   |                               | x  |
| <b>OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)</b>   |    |  |   |   |   |  |   |                           |            |                    |       |          |                               |    |
|   | LI | Amass et al., "Efficacy of daily and alternate-day dosing regimens with the combination buprenorphine-naloxone tablet"; Drug and Alcohol Dependence (2000) Vol 58, pp. 143-152.  |   |   |   |  |   |                           |            |                    |       |          |                               |    |
|   | LJ | Hassain et al., "Buccal and oral bioavailability of naloxone and naltrexone in rats"; (1987) Vol 36, pp. 127-130.  |   |   |   |  |   |                           |            |                    |       |          |                               |    |
|   | LK | Jasinski et al., "The human pharmacology and abuse potential of N-allylnoroxymorphone naloxone"; J. Pharm and Exper Thera (1967) Vol 157, No 2, pp. 420-426.   |   |   |   |  |   |                           |            |                    |       |          |                               |    |
|   | LM | Jones et al., "Nalmefene: blockade of intravenous morphine challenge effects in opioid abusers in humans"; Drug and Alcohol Dependence (2000) Vol 60, pp. 29-37.   |   |   |   |  |   |                           |            |                    |       |          |                               |    |
|   | LN | Kanof et al., "Clinical Characteristics of Naloxone-Precipitated Withdrawal in Human Opioid-Dependent Subjects"; J Pharma and Exper Thera (1992) Vol 260, No. 1, pp. 355-363.  |   |   |   |  |   |                           |            |                    |       |          |                               |    |
|   | LO | King et al., "Naltrexone Biotransformation and Incidence of Subjective Side Effects: A Preliminary Study"; Alcoholism: Clin and Exper Res (1997) Vol 21, No 5, pp. 906-909.  |   |   |   |  |   |                           |            |                    |       |          |                               |    |
|   | LP | Kogan et al., "Estimation of the Systemic Availability and Other Pharmacokinetic Parameters of Naltrexone in Man after Acute and Chronic Oral Administration"; Res. Comm. In Chem. Path. And Pharm (1977) Vol 18, No. 1, pp 29-34. |   |   |   |  |   |                           |            |                    |       |          |                               |    |
|   | LQ | Kosten, Thomas R., M.D., "Buprenorphine for Benzodiazepine-Abusing Heroin Addicts"; Amer J of Psychiatry (1994) Vol 1, p 151.  |   |   |   |  |   |                           |            |                    |       |          |                               |    |
|   | LR | Kosten et al., "Opioid antagonist challenges in buprenorphine maintained patients"; Drug and Alcohol Dependence (1990) Vol 25, OO. 73-78.  |   |   |   |  |   |                           |            |                    |       |          |                               |    |
|   | LS | Kurland et al., "Naloxone and the Narcotic Abuser: A Controlled Study of Partial Blockade"; Inter. J. of the Addictions (1974) Vol 9, No 5, pp. 663-672.   |   |   |   |  |   |                           |            |                    |       |          |                               |    |
| EXAMINER  |    |  |   |   |   |  |   |                           |            | DATE CONSIDERED    |       |          |                               |    |
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|   | MA | 5  | 4 | 6  | 0 | 8                         | 2 | 6    | 10/24/1995      | Merrill et al.  | 424      | 470                           |  |
|   | MB | 5  | 4 | 7  | 2 | 2                         | 1 | 2    | 12/05/1995      | Oshlack et al.  | 424      | 480                           |  |
|   | ME | 5  | 4 | 7  | 2 | 0                         | 4 | 3    | 12/95           | Crain et al.    | 514      | 12                            |  |
|   | MD | 5  | 4 | 7  | 4 | 5                         | 7 | 7    | 12/26/1995      | Sackler et al.  | 424      | 489                           |  |
|   | ME | 5  | 4 | 8  | 4 | 3                         | 6 | 2    | 1/96            | Kitchell et al. | 424      | 426                           |  |
|   | MF | 5  | 5 | 0  | 0 | 2                         | 2 | 7    | 03/19/1996      | Oshlack et al.  | 424      | 489                           |  |
| <b>FOREIGN PATENT DOCUMENTS</b>   |    |  |   |  |   |                           |   |      |                 |                 |          |                               |  |
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|   | MG |  |   |  |   |                           |   |      |                 |                 |          |                               |  |
| <b>OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)</b>   |    |  |   |  |   |                           |   |      |                 |                 |          |                               |  |
|   | MH | Lee et al., "Nalbuphine Coadministered with Morphine Prevents Tolerance and Dependence"; Anesth Analg (1997) Vol 84, pp.810-815  |   |  |   |                           |   |      |                 |                 |          |                               |  |
|   | MN | Lehman, et al., "Influence of Naloxone on the Postoperative Analgesic and Respiratory effects of Buprenorphine"; Eur. J. Clin Pharm (1988) Vol 34, pp. 343-352.                                  |   |  |   |                           |   |      |                 |                 |          |                               |  |
|   | MJ | Levine et al., "Potentiation of Pentazocine Analgesia by Low-dose Naloxone"; J Clin Invest (1988) Vol 82, pp. 1574-1577.   |   |  |   |                           |   |      |                 |                 |          |                               |  |
|   | MK | Loimer et al., "Combined Naloxone/Methadone Preparations for Opiate Substitution Therapy"; J. of Substance Abuse Treatment (1991) Vol 8, pp. 157-160.  |   |  |   |                           |   |      |                 |                 |          |                               |  |
|   | ML | Martin et al. "Bioavailability Investigation of a New Tilidine/Naloxone Liquid Formulation Compared to a Reference Formulation"; Arzneim-Forsch./Drug Res. (1999) Vol 49, pp. 599-607.           |   |  |   |                           |   |      |                 |                 |          |                               |  |
|   | MM | Martin et al., "Demonstration of Tolerance to and Physical Dependence on N-allylnormorphine (Nalorphine)"; J. Of Pharm and Exper Thera (1965) Vol 150, No 3. Pp. 437-442.                        |   |  |   |                           |   |      |                 |                 |          |                               |  |
|   | MN | Mendelson et al., "Buprenorphine and naloxone combinations: the effects of three dose ratios in morphine stabilized, opiate-dependent volunteers"; Psychopharmacology (1999) Vol 141, pp. 37-46. |   |  |   |                           |   |      |                 |                 |          |                               |  |
|   | MO | Mendelson et al., "Buprenorphine and naloxone Interactions in Methadone Maintenance Patients"; Society of Biological Psychiatry (1997) Vol 41, pp. 1095-1101.                                    |   |  |   |                           |   |      |                 |                 |          |                               |  |
|   | MP | Nutt et al., "Methadone-naloxone mixture for use in methadone maintenance programs"; Clin Pharm and Ther. Vol 15, No 2., pp 156-166  |   |  |   |                           |   |      |                 |                 |          |                               |  |
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|   | NA | 5   | 5 | 0 | 2 | 0  | 5 | 8                         | 3/96       | Mayer et al.    | 514   | 289      |                               |    |
|   | NB | 5   | 5 | 0 | 8 | 4  | 1 | 2                         | 04/16/1996 | Oshlack et al.  | 424   | 468      |                               |    |
|   | NC | 5   | 5 | 0 | 8 | 0  | 4 | 3                         | 04/16/1996 | Krishnamurthy   | 424   | 484      |                               |    |
|   | ND | 5   | 5 | 1 | 2 | 5  | 7 | 8                         | 4/96       | Crain et al.    | 514   | 282      |                               |    |
|   | NE | 5   | 5 | 1 | 4 | 6  | 8 | 0                         | 5/96       | Weber et al.    | 514   | 249      |                               |    |
| <b>FOREIGN PATENT DOCUMENTS</b>   |    |   |   |   |   |  |   |                           |            |                 |       |          |                               |    |
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|   | NE |   |   |   |   |  |   |                           |            |                 |       |          |                               |    |
| <b>OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)</b>   |    |   |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   | NG | Parwatar et al., "Methadone-naloxone in combination for the Treatment of Heroin Addicts"; Clin. Pharm and Thera, Vol 14, No. 6, pp 941-948.   |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   | NH | Parwatar et al., "Naloxone-Methadone Combination for the Treatment of Opiate Dependence"; Missouri Institute of Psychiatry, pp. 1350-1354.  |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   | NI | Pitts et al., "Antinociceptive and Response Rate-Altering Effects of <i>Kappa</i> Opioid Agonists, Spiradoline, Enadoline and U69,593, Alone and in Combination with Opioid Antagonists in Squirrel Monkeys"; J of Pharm and Exper Thera (1994) Vol 271, No 3, pp. 1501-1508. |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   | NJ | Preston et al., "Buprenorphine and Naloxone alone and in combination in Opioid-dependant Humans"; Psychopharmacology (1988), Vol 94, pp. 484-490.   |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   | NK | Preston et al., "Differential Naltrexone Antagonism of Hydromorphone and Pentazocine Effects in Human Volunteers"; J of Pharm and Exper Thera (1993) Vol 264, No 2 pp. 813-823.   |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   | NJ | Preston et al., "Effects of Sublingually given naloxone in Opioid -dependant human volunteers"; Drug and Alcohol Dependence (1990) Vol 25, pp. 27-34.   |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   | NM | Bigelow et al., "Abuse Liability and Assessment of Buprenorphine-Naloxone Combinations"; Dept of Psychiatry and Behavioral Sciences, The Johns Hopkins University School of Medicine, pp. 145-149.  |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   | NN | Wikler et al., "N-Allylnormorphine: Effects of single dose and Precipitation of Acute "Abstinence Syndromes" during addiction to morphine, methadone or heroin in man (post addicts)"; N-Allylnormorphine During Narcotic Addiction (1953) pp. 8-20.                          |   |   |   |  |   |                           |            |                 |       |          |                               |    |
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|   | OA | 5   | 5 | 3  | 4 | 4                         | 9 | 2 | 7/96       | Aston et al.    | 514   | 608      |                               |    |
|   | OB | 5   | 5 | 4  | 9 | 9                         | 1 | 2 | 08/27/1996 | Oshlack et al.  | 424   | 468      |                               |    |
|   | OC | 5   | 5 | 5  | 2 | 4                         | 2 | 2 | 09/03/1996 | Gauthier et al. | 514   | 368      |                               |    |
|   | OD | 5   | 5 | 5  | 6 | 8                         | 3 | 8 | 9/96       | Mayer et al.    | 514   | 25       |                               |    |
|   | OL | 5   | 5 | 7  | 4 | 0                         | 5 | 2 | 11/96      | Rose et al.     | 514   | 343      |                               |    |
| <b>FOREIGN PATENT DOCUMENTS</b>   |    |   |   |  |   |                           |   |   |            |                 |       |          |                               |    |
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|   | OG | Zaks et al., "Naloxone Treatment of Opiate Dependence"; JAMA (1971) Vol 215, No 13, pp. 2108-2110.  |   |  |   |                           |   |   |            |                 |       |          |                               |    |
|   | OH | Barton, et al., "Intranasal Administration of Naloxone by Paramedics"; Prehospital Emergency Care (2002) Vol 6, No 1, pp. 54-58.  |   |  |   |                           |   |   |            |                 |       |          |                               |    |
|   | OI | Blachly, Paul, H., M.D., "Naloxone in Opiate Addiction"; Current Psychiatric Therapies (1976) pp. 209-213.  |   |  |   |                           |   |   |            |                 |       |          |                               |    |
|   | OJ | Bashaw et al., "Relative bioavailability of controlled-release oral morphine sulfate during naltrexone blockade"; Inter J of Clin Pharm and Thera (1995) Vol 33, No 9, 524-529.   |   |  |   |                           |   |   |            |                 |       |          |                               |    |
|   | OK | Jasinski, D.R., "Assessment of the Abuse Potentiality of Morphinelike Drugs (Methods Used in Man)"; Drug Addiction (1977) pp. 197-258.  |   |  |   |                           |   |   |            |                 |       |          |                               |    |
|   | OL | Johnson et al., "Buprenorphine and Naloxone for Heroin Dependence"; Substance Use Disorders (2000) pp. 519-526.   |   |  |   |                           |   |   |            |                 |       |          |                               |    |
|   | OM | Strain et al., "Opioid antagonist effects of dezocine in opioid-dependent humans"; Clin Pharm and Thera (1996) Vol 60, No 2, pp. 206-217.   |   |  |   |                           |   |   |            |                 |       |          |                               |    |
|   | ON | Preston et al., "Abuse liability and studies of opioid agonist-antagonists in humans"; Drug and Alcohol Dependence (1991) vol 28, pp. 49-82.  |   |  |   |                           |   |   |            |                 |       |          |                               |    |
|   | OO | Brennscheidt et al., "Pharmacokinetics of Nortilidine and Naloxone after Administration of Tilidine/Naloxone Solution or Tilidine/Naloxone Sustained Release Tablets"; Arzneim-Forsch/Drug Res. (2000) Vol 50, pp. 1015-1022. |   |  |   |                           |   |   |            |                 |       |          |                               |    |
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|   | PA | 5  | 5 | 7 | 8 | 7  | 2 | 5                         | 11/96      | Portoghese et al. | 546   | 35       |                               |    |
|   | PB | 5  | 5 | 8 | 0 | 8  | 7 | 6                         | 12/96      | Crain et al.      | 514   | 282      |                               |    |
|   | PC | 5  | 5 | 8 | 5 | 3  | 4 | 8                         | 12/96      | Crain et al.      | 514   | 12       |                               |    |
|   | PD | 5  | 5 | 9 | 1 | 4  | 5 | 2                         | 01/04/1997 | Miller et al.     | 424   | 468      |                               |    |
|   | PE | 5  | 6 | 0 | 1 | 8  | 4 | 5                         | 02/11/1997 | Buxton et al.     | 424   | 495      |                               |    |
| <b>FOREIGN PATENT DOCUMENTS</b>   |    |  |   |   |   |  |   |                           |            |                   |       |          |                               |    |
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|   | PF |  |   |   |   |  |   |                           |            |                   |       |          |                               |    |
| <b>OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)</b>   |    |  |   |   |   |  |   |                           |            |                   |       |          |                               |    |
|   | PG | Benfey, "Function of Myocardial $\alpha$ -Adrenoceptors"; Life Sciences (1982) vol 31, pp. 101-112.  |   |   |   |  |   |                           |            |                   |       |          |                               |    |
|   | PH | Levine et al., "Potentiation of Pentazocine Analgesia by Low-dose Naloxone"; J of Clin Invest. (1988) Vol 82, pp. 1547-1577.   |   |   |   |  |   |                           |            |                   |       |          |                               |    |
|   | PI | Yoburn et al., "Opioid Antagonist-induced Receptor Upregulation: Effects of Concurrent Agonist Administration"; Brain Research Bulletin (1994), Vol 33, pp. 237-240.   |   |   |   |  |   |                           |            |                   |       |          |                               |    |
|   | PJ | Bunzow et al., "Molecular Cloning and Tissue Distribution of a Putative Member of the Rat Opioid Receptor Gene Family that is not a $\mu$ , $\delta$ , or $\kappa$ opioid receptor type"; FEBS letters (1994) pp. 284-288. |   |   |   |  |   |                           |            |                   |       |          |                               |    |
|   | PK | Mollereau et al., "ORL 1, a novel member of the opioid receptor family: Cloning, functional expression and localization"; FEBS letters 341 (1994), pp. 33-38.  |   |   |   |  |   |                           |            |                   |       |          |                               |    |
|   | PL | Wang, et al., "cDNA cloning of an orphan opiate receptor gene family member and its splice variant"; FEBS letters 348 (1994) pp. 75-79.  |   |   |   |  |   |                           |            |                   |       |          |                               |    |
|   | PM | Suzuki et al., "Morphine conditioned place preference after chronic treatment with naloxone in the rat"; Research Communications in Substance Abuse (1991) vol 12., No 3., pp. 119-131.                                    |   |   |   |  |   |                           |            |                   |       |          |                               |    |
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| *EXAMINER<br>INITIAL  |    | DOCUMENT NUMBER   |   |   |  |   |                           |   | DATE       | NAME            | CLASS | SUBCLASS | FILING DATE<br>IF APPROPRIATE |    |
|   | QA | 5   | 6 | 1 | 4  | 6 | 6                         | 1 | 4/97       | Khanna et al.   | 514   | 399      |                               |    |
|   | QB | 5   | 4 | 2 | 2  | 7 | 2                         | 2 | 04/22/1997 | Knott et al.    | 424   | 494      |                               |    |
|   | QC | 5   | 6 | 2 | 4  | 9 | 3                         | 2 | 4/97       | Qin et al.      | 514   | 282      |                               |    |
|   | QD | 5   | 6 | 3 | 3  | 2 | 5                         | 9 | 5/97       | Qin et al.      | 514   | 282      |                               |    |
|   | QE | 5   | 6 | 3 | 9  | 4 | 7                         | 6 | 06/17/1997 | Oshlack et al.  | 424   | 468      |                               |    |
| <b>FOREIGN PATENT DOCUMENTS</b>   |    |   |   |   |  |   |                           |   |            |                 |       |          |                               |    |
|   |    | DOCUMENT NUMBER   |   |   |  |   |                           |   | DATE       | COUNTRY         | CLASS | SUBCLASS | TRANSLATION                   |    |
|   |    |   |   |   |  |   |                           |   |            |                 |       |          | YES                           | NO |
|   | QF |   |   |   |  |   |                           |   |            |                 |       |          |                               |    |
| <b>OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)</b>   |    |   |   |   |  |   |                           |   |            |                 |       |          |                               |    |
|   | QG | Press Release "International Patent Application to Be Published on Abuse-Resistant Pain Reliever Being Developed by Perdue Pharma"; August 8, 2001.   |   |   |  |   |                           |   |            |                 |       |          |                               |    |
|   | QI | Paronis et al., "Increased Analgesic Potency of Mu Agonists after Continuous Naloxone Infusion in Rats"; J of Pharm Exper Thera (1991), 259 (2), pp. 582-589.   |   |   |  |   |                           |   |            |                 |       |          |                               |    |
|   | QI | Yoburn et al., "Supersensitivity to Opioid Analgesics Following Chronic Opioid Antagonist Treatment: Relationship to Receptor Sensitivity"; Pharmacology Bio Beh (1995) Vol 51 No. 2, pp. 535-539.            |   |   |  |   |                           |   |            |                 |       |          |                               |    |
|   | QI | Crain et al., "Acute thermal hyperalgesia elicited by low-dose morphine in normal mice is blocked by ultra-low-dose naltrexone, unmasking potent opioid analgesia"; Brain Research (2001) Vol 888, pp. 75-82. |   |   |  |   |                           |   |            |                 |       |          |                               |    |
|   | QI | Zhang et al., "Down-Regulation of $\mu$ -Opioid Receptors in Rat and Monkey Dorsal Root Ganglion Neurons and Spinal Cord After Peripheral Axotomy"; Neuroscience (1998) Vol 82., pp. 223-240.                 |   |   |  |   |                           |   |            |                 |       |          |                               |    |
|   | QI | Abdulla et al., "Axotomy reduces the effect of analgesic opioids yet increases the effect of nociceptin on dorsal root ganglion neurons"; J of Neuro Sci (1998) Vol 18, pp 9685-9694.                         |   |   |  |   |                           |   |            |                 |       |          |                               |    |
|   | QM | Di Giannuario et al., "Orphanin FQ reduces morphine-induced dopamine release in the nucleus accumbens: a microdialysis study in rats"; Neurosci. Lett (1999) Vol 272 pp. 183-186.                             |   |   |  |   |                           |   |            |                 |       |          |                               |    |
| EXAMINER  |    |   |   |   |  |   |                           |   |            | DATE CONSIDERED |       |          |                               |    |
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|---|----|---|----|----|----|--|---|---------------------------|------------|-----------------|-------|----------|-------------------------------|----|
| FORM PTO-1449<br>(REV. 7-80)  |    | U.S. DEPARTMENT OF COMMERCE<br>PATENT AND TRADEMARK OFFICE  |    |    |    | ATTY. DOCKET NO.:<br>200.1134CON         |   | SERIAL NO.:<br>10/747,865 |            |                 |       |          |                               |    |
| <b>LIST OF PRIOR ART CITED BY APPLICANT</b><br><br>(Use several sheets if necessary)  |    |   |    |    |    | APPLICANT(S):<br>Benjamin OSHLACK et al. |   |                           |            |                 |       |          |                               |    |
|   |    |   |    |    |    | FILING DATE:<br>December 29, 2003        |   | GROUP:<br>1614            |            |                 |       |          |                               |    |
| <b>U.S. PATENT DOCUMENTS</b>  |    |   |    |    |    |  |   |                           |            |                 |       |          |                               |    |
| *EXAMINER<br>INITIAL  |    | DOCUMENT NUMBER   |    |    |    |  |   |                           | DATE       | NAME            | CLASS | SUBCLASS | FILING DATE<br>IF APPROPRIATE |    |
|   | RA | 5   | 6  | 5  | 6  | 2  | 9 | 5                         | 08/12/1997 | Oshalck et al.  | 424   | 468      |                               |    |
|   | RB | 5   | 6  | 7  | 0  | 1  | 7 | 2                         | 09/23/1997 | Buxton et al.   | 424   | 495      |                               |    |
|   | RC | 5   | 6  | 7  | 2  | 3  | 6 | 0                         | 09/30/1997 | Sackler et al.  | 424   | 490      |                               |    |
|   | RD | 5   | 6  | 8  | 1  | 5  | 8 | 5                         | 10/28/1997 | Oshlack et al.  | 424   | 494      |                               |    |
|   | RE | 5   | 7  | 6  | 3  | 4  | 5 | 2                         | 06/09/1998 | Miller et al.   | 514   | 282      |                               |    |
|   | RF | 5   | 7  | 6  | 7  | 1  | 2 | 5                         | 06/98      | Crain et al.    | 514   | 282      |                               |    |
|   | RG | 5   | 7  | 8  | 0  | 4  | 7 | 9                         | 07/14/1998 | Kim             | 514   | 282      |                               |    |
|   | RH | 5   | 7  | 6  | 7  | 1  | 2 | 5                         | 06/16/1988 | Crain, et al.   | 514   | 282      |                               |    |
|   | RI | 6   | 0  | 9  | 6  | 7  | 5 | 6                         | 08/01/2000 | Crain, et al.   | 514   | 282      |                               |    |
|   | RJ | 6   | 1  | 9  | 4  | 3  | 8 | 2                         | 02/27/01   | Crain, et al.   | 514   | 2        |                               |    |
|   | RK | 6   | 3  | 6  | 2  | 1  | 9 | 4                         | 03/26/2002 | Crain, et al.   | 514   | 285      |                               |    |
|   | RL | 6   | 3  | 9  | 5  | 7  | 0 | 5                         | 05/28/2002 | Crain, et al.   | 514   | 2        |                               |    |
|   | RM | 20  | 01 | 00 | 06 | 9  | 6 | 7                         | 07/05/2001 | Crain, et al.   | 514   | 253.04   |                               |    |
|   | RN | 20  | 01 | 00 | 18 | 4  | 1 | 3                         | 08/30/2001 | Crain, et al.   | 514   | 2        |                               |    |
| <b>FOREIGN PATENT DOCUMENTS</b>   |    |   |    |    |    |  |   |                           |            |                 |       |          |                               |    |
|   |    | DOCUMENT NUMBER   |    |    |    |  |   |                           | DATE       | COUNTRY         | CLASS | SUBCLASS | TRANSLATION                   |    |
|   |    |   |    |    |    |  |   |                           |            |                 |       |          | YES                           | NO |
|   | RO |   |    |    |    |  |   |                           |            |                 |       |          |                               |    |
| <b>OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)</b>   |    |   |    |    |    |  |   |                           |            |                 |       |          |                               |    |
|   | RP | Ciccocioppo et al., "Effect of Nociceptin/orphanin FQ on the Rewarding Properties of Morphine"; Eur. J Pharmacol (2000) Vol 404, pp. 153-159. |    |    |    |  |   |                           |            |                 |       |          |                               |    |
|   | RQ | Physician's Desk Reference (2001) see Revia, pp. 1146-1149 and Oxycontin, pp. 2697-2701   |    |    |    |  |   |                           |            |                 |       |          |                               |    |
|   | RR |   |    |    |    |  |   |                           |            |                 |       |          |                               |    |
|   | RS |   |    |    |    |  |   |                           |            |                 |       |          |                               |    |
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|---|----|--|---|---|---|--|---|---------------------------|------------|-------------------|-------|----------|-------------------------------|----|
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|   |    |  |   |   |   | FILING DATE:<br>December 29, 2003        |   | GROUP:<br>1614            |            |                   |       |          |                               |    |
| U.S. PATENT DOCUMENTS   |    |  |   |   |   |  |   |                           |            |                   |       |          |                               |    |
| *EXAMINER<br>INITIAL  | SA | 5  | 8 | 1 | 1 | 1  | 2 | 6                         | DATE       | NAME              | CLASS | SUBCLASS | FILING DATE<br>IF APPROPRIATE |    |
|   | SA | 5  | 8 | 1 | 1 | 1  | 2 | 6                         | 09/22/1998 | Krishnamurthy     | 424   | 498      |                               |    |
|   | SB | 5  | 8 | 3 | 4 | 4  | 7 | 7                         | 11/10/1998 | Mioduszewski      | 514   | 282      |                               |    |
|   | SC | 5  | 8 | 4 | 3 | 4  | 8 | 0                         | 12/01/1998 | Miller et al.     | 424   | 484      |                               |    |
|   | SD | 5  | 8 | 4 | 9 | 2  | 4 | 0                         | 12/15/1998 | Miller et al.     | 264   | 460      |                               |    |
|   | SE | 5  | 8 | 5 | 8 | 0  | 1 | 7                         | 1/99       | Demopoulos et al. | 604   | 890.1    |                               |    |
|   | SF | 5  | 8 | 6 | 0 | 9  | 5 | 0                         | 1/99       | Demopoulos et al. | 604   | 49       |                               |    |
|   | SG | 5  | 8 | 6 | 6 | 1  | 6 | 4                         | 2/99       | Kuczynski et al.  | 424   | 472      |                               |    |
|   | SH | 5  | 4 | 0 | 9 | 9  | 4 | 4                         | 04/25/1995 | Black et al.      | 514   | 359      |                               |    |
|   | SI | 5  | 1 | 3 | 0 | 3  | 1 | 1                         | 07/14/1992 | Guillaumet et al. | 514   | 234.2    |                               |    |
|   | SJ | 4  | 4 | 0 | 1 | 6  | 7 | 2                         | 08/30/1983 | Portoghese        | 424   | 260      |                               |    |
|   | SK | 4  | 4 | 5 | 7 | 9  | 3 | 3                         | 07/03/1984 | Gordon et al.     | 424   | 260      |                               |    |
|   | SL | 5  | 4 | 3 | 6 | 7  | 6 | 5                         | 07/25/1995 | Black et al.      | 514   | 420      |                               |    |
|   | SM | 5  | 6 | 3 | 9 | 7  | 8 | 0                         | 06/17/1997 | Lau et al.        | 514   | 419      |                               |    |
|   | SN | 5  | 6 | 0 | 4 | 2  | 6 | 0                         | 02/18/1997 | Guay et al.       | 514   | 605      |                               |    |
|   | SO | 5  | 6 | 0 | 4 | 2  | 5 | 3                         | 02/18/1997 | Lau et al.        | 514   | 415      |                               |    |
|   | SP | 5  | 5 | 9 | 3 | 9  | 9 | 4                         | 01/14/1997 | Batt et al.       | 514   | 252      |                               |    |
|   | SQ | 5  | 5 | 3 | 6 | 7  | 5 | 2                         | 07/16/1996 | Ducharme et al.   | 514   | 602      |                               |    |
|   | SR | 5  | 5 | 5 | 0 | 1  | 4 | 2                         | 08/27/1996 | Ducharme et al.   | 514   | 365      |                               |    |
|   | SS | 5  | 5 | 7 | 1 | 2  | 1 | 3                         | 05/28/1996 | Prasit et al.     | 514   | 443      |                               |    |
|   | ST | 5  | 5 | 1 | 0 | 3  | 6 | 8                         | 04/23/1996 | Lau et al.        | 514   | 419      |                               |    |
|   | SU | 5  | 4 | 7 | 4 | 5  | 5 | 5                         | 12/12/1995 | Ducharme et al.   | 514   | 241      |                               |    |
| FOREIGN PATENT DOCUMENTS  |    |  |   |   |   |  |   |                           |            |                   |       |          |                               |    |
|   |    | DOCUMENT NUMBER  |   |   |   |  |   |                           | DATE       | COUNTRY           | CLASS | SUBCLASS | TRANSLATION                   |    |
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|   | SX |  |   |   |   |  |   |                           |            |                   |       |          |                               |    |
| OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)  |    |  |   |   |   |  |   |                           |            |                   |       |          |                               |    |
|   | SY |  |   |   |   |  |   |                           |            |                   |       |          |                               |    |
| EXAMINER  |    |  |   |   |   |  |   |                           |            | DATE CONSIDERED   |       |          |                               |    |
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|---|----|--|---|---|---|--|---|---------------------------|------------|-----------------|-------|----------|-------------------------------|----|
| FORM PTO-1449<br>(REV. 7-80)  |    | U.S. DEPARTMENT OF COMMERCE<br>PATENT AND TRADEMARK OFFICE |   |   |   | ATTY. DOCKET NO.:<br>200.1134CON         |   | SERIAL NO.:<br>10/747,865 |            |                 |       |          |                               |    |
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|   |    |  |   |   |   | FILING DATE:<br>December 29, 2003        |   | GROUP:<br>1614            |            |                 |       |          |                               |    |
| <b>U.S. PATENT DOCUMENTS</b>  |    |  |   |   |   |  |   |                           |            |                 |       |          |                               |    |
| *EXAMINER<br>INITIAL  |    | DOCUMENT NUMBER  |   |   |   |  |   |                           | DATE       | NAME            | CLASS | SUBCLASS | FILING DATE<br>IF APPROPRIATE |    |
|   | TA | 5  | 8 | 6 | 9 | 0  | 9 | 7                         | 02/09/1999 | Wong et al.     | 424   | 473      |                               |    |
|   | TB | 5  | 8 | 7 | 9 | 7  | 0 | 5                         | 03/09/1999 | Heafield et al. | 424   | 464      |                               |    |
|   | TC | 5  | 8 | 8 | 0 | 1  | 3 | 2                         | 3/99       | Hill            | 514   | 282      |                               |    |
|   | TD | 5  | 8 | 9 | 1 | 4  | 7 | 1                         | 04/06/1999 | Miller et al.   | 424   | 468      |                               |    |
|   | TE | 5  | 9 | 0 | 8 | 8  | 4 | 8                         | 06/01/1999 | Miller et al.   | 514   | 282      |                               |    |
|   | TF | 5  | 9 | 4 | 2 | 2  | 4 | 1                         | 8/99       | Chasin et al.   | 424   | 426      |                               |    |
|   | TG | 5  | 9 | 5 | 8 | 4  | 5 | 2                         | 09/28/1999 | Oshlack et al.  | 424   | 457      |                               |    |
|   | TH | 3  | 8 | 4 | 5 | 7  | 7 | 0                         | 11/05/1974 | Theeuwes et al. | 128   | 260      |                               |    |
|   | TI | 4  | 0 | 6 | 3 | 0  | 6 | 4                         | 12/13/1977 | Saunders et al. | 219   | 121      |                               |    |
|   | TJ | 4  | 0 | 8 | 8 | 8  | 6 | 4                         | 05/09/1978 | Theeuwes et al. | 219   | 121      |                               |    |
|   | TK | 4  | 2 | 9 | 3 | 5  | 3 | 9                         | 10/06/1981 | Ludwig et al.   | 429   | 19       |                               |    |
|   | TL | 4  | 9 | 5 | 7 | 6  | 8 | 1                         | 09/18/1990 | Klimesch et al. | 264   | 211.23   |                               |    |
| <b>FOREIGN PATENT DOCUMENTS</b>   |    |  |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   |    | DOCUMENT NUMBER  |   |   |   |  |   |                           | DATE       | COUNTRY         | CLASS | SUBCLASS | TRANSLATION                   |    |
|   |    |  |   |   |   |  |   |                           |            |                 |       |          | YES                           | NO |
|   | TM |  |   |   |   |  |   |                           |            |                 |       |          |                               |    |
| <b>OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)</b>   |    |  |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   | TN |  |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   | TO |  |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   | TP |  |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   | TQ |  |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   | TR |  |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   | TS |  |   |   |   |  |   |                           |            |                 |       |          |                               |    |
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|   |    |  |   |   |   | FILING DATE:<br>December 29, 2003        |   | GROUP:<br>1614            |            |                 |       |          |                               |    |
| <b>U.S. PATENT DOCUMENTS</b>  |    |  |   |   |   |  |   |                           |            |                 |       |          |                               |    |
| *EXAMINER<br>INITIAL  |    | DOCUMENT NUMBER  |   |   |   |  |   |                           | DATE       | NAME            | CLASS | SUBCLASS | FILING DATE<br>IF APPROPRIATE |    |
|   | UA | 5  | 9 | 5 | 8 | 4  | 5 | 9                         | 09/28/1999 | Chasin et al.   | 424   | 490      |                               |    |
|   | UB | 5  | 9 | 6 | 5 | 1  | 6 | 1                         | 10/12/1999 | Oshlack et al.  | 424   | 457      |                               |    |
|   | UC | 5  | 9 | 6 | 5 | 1  | 6 | 3                         | 10/12/1999 | Miller et al.   | 424   | 468      |                               |    |
|   | UD | 5  | 9 | 6 | 8 | 5  | 4 | 7                         | 10/99      | Reder et al.    | 424   | 449      |                               |    |
|   | UE | 5  | 9 | 6 | 8 | 5  | 5 | 1                         | 10/19/1999 | Oshlack et al.  | 424   | 456      |                               |    |
|   | UF | 5  | 9 | 7 | 2 | 9  | 5 | 4                         | 10/99      | Foss            | 514   | 282      |                               |    |
|   | UG | 5  | 9 | 9 | 8 | 4  | 3 | 4                         | 12/99      | Mitch et al.    | 514   | 210.16   |                               |    |
|   | UH | 3  | 1 | 7 | 3 | 8  | 7 | 7                         | 03/16/1965 | Jackson et al.  | 252   | 138      |                               |    |
|   | UI | 4  | 5 | 8 | 7 | 1  | 1 | 8                         | 05/06/1986 | Hsiao           | 424   | 459      |                               |    |
| <b>FOREIGN PATENT DOCUMENTS</b>   |    |  |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   |    | DOCUMENT NUMBER  |   |   |   |  |   |                           | DATE       | COUNTRY         | CLASS | SUBCLASS | TRANSLATION                   |    |
|   |    |  |   |   |   |  |   |                           |            |                 |       |          | YES                           | NO |
|   | UJ | 04   | 0 | 5 | 2 | 3  | 4 | 6                         | 06/24/2004 | WO(A1)          | A61K  | 9/62     |                               |    |
|   | UK | 0  | 5 | 4 | 8 | 4  | 4 | 8                         | 09/06/2000 | EP (B1)         | A61K  | 9/50     | abstract                      |    |
|   | UL | 9  | 9 | 1 | 3 | 7  | 9 | 9                         | 03/25/1999 | WO (A1)         | A61F  | 2/02     |                               |    |
| <b>OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)</b>   |    |  |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   | UM |  |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   | UN |  |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   | UO |  |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   | UP |  |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   | UQ |  |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   | UR |  |   |   |   |  |   |                           |            |                 |       |          |                               |    |
|   | US |  |   |   |   |  |   |                           |            |                 |       |          |                               |    |
| EXAMINER  |    |  |   |   |   |  |   |                           |            | DATE CONSIDERED |       |          |                               |    |
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|   |    |  |   | FILING DATE:<br>December 29, 2003        |   | GROUP:<br>1614            |   |   |            |                  |       |          |                               |    |
| <b>U.S. PATENT DOCUMENTS</b>  |    |  |   |  |   |                           |   |   |            |                  |       |          |                               |    |
| *EXAMINER<br>INITIAL  |    | DOCUMENT NUMBER  |   |  |   |                           |   |   | DATE       | NAME             | CLASS | SUBCLASS | FILING DATE<br>IF APPROPRIATE |    |
|   | VA | 6  | 0 | 2  | 4 | 9                         | 8 | 2 | 02/15/2000 | Oshlack et al.   | 424   | 476      |                               |    |
|   | VB | 6  | 0 | 6  | 8 | 8                         | 5 | 5 | 05/30/2000 | Leslie et al.    | 424   | 468      |                               |    |
|   | VC | 6  | 0 | 7  | 7 | 5                         | 3 | 2 | 06/20/2000 | Malkowska et al. | 424   | 457      |                               |    |
|   | VD | 6  | 0 | 7  | 7 | 5                         | 3 | 3 | 06/20/2000 | Oshlack et al.   | 424   | 461      |                               |    |
|   | VE | 6  | 1 | 0  | 3 | 2                         | 5 | 8 | 08/15/2000 | Simon            | 424   | 449      |                               |    |
|   | VF | 6  | 1 | 0  | 3 | 2                         | 6 | 1 | 08/15/2000 | Chasin et al.    | 424   | 459      |                               |    |
|   | VG | 6  | 1 | 4  | 3 | 3                         | 2 | 2 | 11/07/2000 | Sackler et al    | 424   | 459      |                               |    |
| <b>FOREIGN PATENT DOCUMENTS</b>   |    |  |   |  |   |                           |   |   |            |                  |       |          |                               |    |
|   |    | DOCUMENT NUMBER  |   |  |   |                           |   |   | DATE       | COUNTRY          | CLASS | SUBCLASS | TRANSLATION                   |    |
|   |    |  |   |  |   |                           |   |   |            |                  |       |          | YES                           | NO |
|   | VH |  |   |  |   |                           |   |   |            |                  |       |          |                               |    |
|   | VI |  |   |  |   |                           |   |   |            |                  |       |          |                               |    |
|   | VJ |  |   |  |   |                           |   |   |            |                  |       |          |                               |    |
|   | VK |  |   |  |   |                           |   |   |            |                  |       |          |                               |    |
|   | VL |  |   |  |   |                           |   |   |            |                  |       |          |                               |    |
| <b>OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)</b>   |    |  |   |  |   |                           |   |   |            |                  |       |          |                               |    |
|   | VM |  |   |  |   |                           |   |   |            |                  |       |          |                               |    |
|   | VN |  |   |  |   |                           |   |   |            |                  |       |          |                               |    |
|   | VO |  |   |  |   |                           |   |   |            |                  |       |          |                               |    |
|   | VP |  |   |  |   |                           |   |   |            |                  |       |          |                               |    |
|   | VQ |  |   |  |   |                           |   |   |            |                  |       |          |                               |    |
|   | VR |  |   |  |   |                           |   |   |            |                  |       |          |                               |    |
|   | VS |  |   |  |   |                           |   |   |            |                  |       |          |                               |    |
| EXAMINER  |    |  |   |  |   |                           |   |   |            | DATE CONSIDERED  |       |          |                               |    |
| *EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. |    |  |   |  |   |                           |   |   |            |                  |       |          |                               |    |

|   |    |  |   |  |   |                           |   |   |            |                 |       |          |                               |    |
|---|----|--|---|--|---|---------------------------|---|---|------------|-----------------|-------|----------|-------------------------------|----|
| FORM PTO-1449<br>(REV. 7-80)  |    | U.S. DEPARTMENT OF COMMERCE<br>PATENT AND TRADEMARK OFFICE |   | ATTY. DOCKET NO.:<br>200.1134CON         |   | SERIAL NO.:<br>10/747,865 |   |   |            |                 |       |          |                               |    |
| <b>LIST OF PRIOR ART CITED BY APPLICANT</b><br><br>(Use several sheets if necessary)  |    |  |   | APPLICANT(S):<br>Benjamin OSHLACK et al. |   |                           |   |   |            |                 |       |          |                               |    |
|   |    |  |   | FILING DATE:<br>December 29, 2003        |   | GROUP:<br>1614            |   |   |            |                 |       |          |                               |    |
| <b>U.S. PATENT DOCUMENTS</b>  |    |  |   |  |   |                           |   |   |            |                 |       |          |                               |    |
| *EXAMINER<br>INITIAL  |    | DOCUMENT NUMBER  |   |  |   |                           |   |   | DATE       | NAME            | CLASS | SUBCLASS | FILING DATE<br>IF APPROPRIATE |    |
|   | WA | 6  | 1 | 4  | 3 | 3                         | 2 | 8 | 11/07/2000 | Heafield et al. | 424   | 489      |                               |    |
|   | WB | 6  | 1 | 6  | 2 | 4                         | 6 | 7 | 12/19/2000 | Miller et al.   | 424   | 468      |                               |    |
|   | WC | 6  | 2 | 1  | 0 | 7                         | 1 | 4 | 04/03/2001 | Oshlack et al.  | 424   | 476      |                               |    |
|   | WD | 6  | 2 | 2  | 8 | 8                         | 6 | 3 | 05/08/2001 | Palermo et al.  | 514   | 282      |                               |    |
|   | WE | 6  | 2 | 5  | 4 | 8                         | 8 | 7 | 07/03/2001 | Miller et al.   | 424   | 468      |                               |    |
|   | WF | 6  | 2 | 6  | 1 | 5                         | 9 | 9 | 07/17/2001 | Oshlack et al.  | 424   | 457      |                               |    |
|   | WG | 6  | 2 | 7  | 7 | 3                         | 8 | 4 | 08/21/2001 | Kaiko et al.    | 424   | 400      |                               |    |
| <b>FOREIGN P/TENT DOCUMENTS</b>   |    |  |   |  |   |                           |   |   |            |                 |       |          |                               |    |
|   |    | DOCUMENT NUMBER  |   |  |   |                           |   |   | DATE       | COUNTRY         | CLASS | SUBCLASS | TRANSLATION                   |    |
|   |    |  |   |  |   |                           |   |   |            |                 |       |          | YES                           | NO |
|   | WH |  |   |  |   |                           |   |   |            |                 |       |          |                               |    |
|   | WI |  |   |  |   |                           |   |   |            |                 |       |          |                               |    |
|   | WE |  |   |  |   |                           |   |   |            |                 |       |          |                               |    |
|   | WK |  |   |  |   |                           |   |   |            |                 |       |          |                               |    |
|   | WL |  |   |  |   |                           |   |   |            |                 |       |          |                               |    |
| <b>OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)</b>   |    |  |   |  |   |                           |   |   |            |                 |       |          |                               |    |
|   | WM |  |   |  |   |                           |   |   |            |                 |       |          |                               |    |
|   | WN |  |   |  |   |                           |   |   |            |                 |       |          |                               |    |
|   | WO |  |   |  |   |                           |   |   |            |                 |       |          |                               |    |
|   | WP |  |   |  |   |                           |   |   |            |                 |       |          |                               |    |
|   | WQ |  |   |  |   |                           |   |   |            |                 |       |          |                               |    |
|   | WR |  |   |  |   |                           |   |   |            |                 |       |          |                               |    |
|   | WS |  |   |  |   |                           |   |   |            |                 |       |          |                               |    |
| EXAMINER  |    |  |   |  |   |                           |   |   |            | DATE CONSIDERED |       |          |                               |    |
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|---|----|--|---|---|---|--|---|---------------------------|------------|-----------------|-------|----------|-------------------------------|----|--|
| <b>LIST OF PRIOR ART CITED BY APPLICANT</b><br><br>(Use several sheets if necessary)  |    |  |   |   |   | APPLICANT(S):<br>Benjamin OSHLACK et al. |   |                           |            |                 |       |          |                               |    |  |
|   |    |  |   |   |   | FILING DATE:<br>December 29, 2003        |   | GROUP:<br>1614            |            |                 |       |          |                               |    |  |
| <b>U.S. PATENT DOCUMENTS</b>  |    |  |   |   |   |  |   |                           |            |                 |       |          |                               |    |  |
| *EXAMINER<br>INITIAL  |    | DOCUMENT NUMBER  |   |   |   |  |   |                           | DATE       | NAME            | CLASS | SUBCLASS | FILING DATE<br>IF APPROPRIATE |    |  |
|   | XA | 6  | 2 | 9 | 4 | 1  | 9 | 5                         | 09/25/2001 | Oshlack et al.  | 424   | 457      |                               |    |  |
|   | XB | 6  | 3 | 0 | 6 | 4  | 3 | 8                         | 10/23/2001 | Oshlack et al.  | 424   | 468      |                               |    |  |
|   | XC | 6  | 3 | 2 | 6 | 0  | 2 | 7                         | 12/04/2001 | Miller et al.   | 424   | 468      |                               |    |  |
|   | XD | 6  | 3 | 3 | 5 | 0  | 3 | 3                         | 01/01/2002 | Oshlack et al.  | 424   | 457      |                               |    |  |
|   | XE | 6  | 3 | 7 | 5 | 9  | 5 | 7                         | 04/23/2002 | Kaiko et al.    | 424   | 400      |                               |    |  |
|   | XF | 6  | 3 | 8 | 7 | 4  | 0 | 4                         | 05/14/2002 | Oshlack et al.  | 424   | 480      |                               |    |  |
|   | XG | 6  | 3 | 9 | 9 | 0  | 9 | 6                         | 06/04/2002 | Miller et al.   | 424   | 464      |                               |    |  |
|   | XH | 6  | 4 | 7 | 5 | 4  | 9 | 4                         | 11/05/2002 | Kaiko et al.    | 424   | 400      |                               |    |  |
|   | XI | 6  | 6 | 2 | 7 | 6  | 3 | 5                         | 09/30/2003 | Palermo, et al. | 514   | 282      |                               |    |  |
|   | XJ | 6  | 7 | 1 | 6 | 4  | 4 | 9                         | 04/06/2004 | Oshlack, et al. | 424   | 449      |                               |    |  |
|   | XK | 6  | 6 | 9 | 6 | 0  | 8 | 8                         | 02/24/2004 | Oshlack et al.  | 424   | 465      |                               |    |  |
|   | XL | 6  | 6 | 9 | 6 | 0  | 6 | 6                         | 02/24/2004 | Kaiko et al.    | 424   | 400      |                               |    |  |
| <b>FOREIGN PATENT DOCUMENTS</b>   |    |  |   |   |   |  |   |                           |            |                 |       |          |                               |    |  |
|   |    | DOCUMENT NUMBER  |   |   |   |  |   |                           | DATE       | COUNTRY         | CLASS | SUBCLASS | TRANSLATION                   |    |  |
|   |    |  |   |   |   |  |   |                           |            |                 |       |          | YES                           | NO |  |
|   | XM |  |   |   |   |  |   |                           |            |                 |       |          |                               |    |  |
| <b>OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)</b>   |    |  |   |   |   |  |   |                           |            |                 |       |          |                               |    |  |
|   | XN |  |   |   |   |  |   |                           |            |                 |       |          |                               |    |  |
|   | XO |  |   |   |   |  |   |                           |            |                 |       |          |                               |    |  |
|   | XP |  |   |   |   |  |   |                           |            |                 |       |          |                               |    |  |
|   | XQ |  |   |   |   |  |   |                           |            |                 |       |          |                               |    |  |
|   | XR |  |   |   |   |  |   |                           |            |                 |       |          |                               |    |  |
|   | XS |  |   |   |   |  |   |                           |            |                 |       |          |                               |    |  |
|   | XT |  |   |   |   |  |   |                           |            |                 |       |          |                               |    |  |
| EXAMINER  |    |  |   |   |   |  |   |                           |            | DATE CONSIDERED |       |          |                               |    |  |
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